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A COMPARISON OF THE BERGER TEST WITH OTHER SEROLOGICAL TESTS FOR SYPHILIS.

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In 1943 Berger[1] described an agglutination test for the serological diagnosis of syphilis. In this test one makes use of a suspension of collodion particles sensitized with Kahn antigen. The sensitized particles are washed by centrifugation and then suspended in saline solution. This suspension of washed, sensitized particles is mixed with the serum under test and the mixture is observed for agglutination. In a series of 2,452 specimens of serum Berger compared his test with the Wassermann and the Kahn tests. He concluded that the sensitivity of the agglutination test was greater than that of either of the other two tests, but also that the non-specificity was greater.

The object of the present work was to make a comparative study of the Wassermann, Kline and Berger tests as applied to the specimens of serum submitted as a routine measure for examination in general hospital practice. The technical procedures are indicated in the following paragraphs, after which an analysis of the results is made.

The Wassermann Test.

Specimens of serum were inactivated at 56° C. for twenty minutes in a water bath and then diluted with saline solution so that the ratio of serum to saline solution was one to four.

The antigen used was prepared by measuring into a dry flask 0·3 millilitre of heart extract (Commonwealth Serum Laboratories) and 0·2 millilitre of a 1% alcoholic solution of cholesterol. Forty-three millilitres of saline solution were suddenly added. This strength of antigen suspension was twice the strength of the limiting antigenic titre and allowed a comfortable margin from the anticomplementary titre. The ratio of heart extract to cholesterol was that found to give maximum sensitivity. The sensitized sheep's corpuscles consisted of 2% (volume for volume) of washed sheep's corpuscles in 0·85% saline solution, with which 0·35 millilitre *per centum* of hæmolytic amboceptor (Commonwealth Serum Laboratories) had been mixed before the addition of the corpuscles. This represents twice the strength of the limiting hæmolytic titre of amboceptor and allows a comfortable margin from the agglutinating titre.

The complement was titrated in the presence of antigen before each batch of tests.

In the test proper three tubes were used. The back tube was the serum control and contained three minimum hæmolytic doses of complement. The front and middle tubes contained respectively three and six minimum hæmolytic doses of complement. Three hours at 4° C. were allowed for fixation of complement, after which the temperature was brought to 37° C., when the sensitized corpuscles were added. The results were recorded as follows: "–", complete hæmolysis in both tubes; "+", partial inhibition of hæmolysis in the front tube and no inhibition in the middle tube; "++", complete inhibition of hæmolysis in the front tube and no inhibition in the middle tube; "+++", complete inhibition of hæmolysis in the front tube and partial inhibition of hæmolysis in the middle tube; "++++", complete inhibition of hæmolysis in the front and middle tubes.

The Kline Test.

The antigen emulsion was prepared by placing 0·85 millilitre of distilled water in a dry half-ounce bottle, after which 1·25 millilitres of a 1% solution of cholesterol in absolute alcohol were run down the side of the bottle into it, and this combination was mixed by rotating the bottle for fifteen to twenty seconds. Next, 0·1 millilitre of Kline antigen (Commonwealth Serum Laboratories) was run in and the bottle was immediately shaken vigorously in a vertical direction for twenty to thirty seconds. For this manœuvre the bottle was closed by a cork covered

with metal foil. Further dilution with 2·2 millilitres of 0·85% solution followed by shaking for twenty to thirty seconds completed the preparation of this antigen emulsion.

In the test one drop of inactivated serum (0·05 millilitre) was mixed with one drop of Kline antigen emulsion (0·03 millilitre). The mixture was rotated by means of a mechanical Kline rotator for four minutes and examined for agglutination under the low power of the microscope. The results were recorded as follows: "–", no observed agglutination (homogeneous suspension of crystals); "+", small clumps of crystals; "++", larger clumps of crystals (eight to twenty clumps per field); "+++", still larger clumps of crystals (three to eight clumps per field); "++++", crystals all in very large clumps (one to three masses per field).

TABLE I.

Subdivision of Positively Reacting Sera ("+", "++", "+++" or "++++" Reaction).

Class.	Number of Cases.
Class I. "Progress" patients ..	199
Class II. Probably syphilitic	72
Class III. Probably not syphilitic ..	85
Class IV. Doubtfully syphilitic ..	26
Class V. No information available ..	44
Total	426

The Berger Test.

Collodion particles were prepared by dissolving 10 grammes of anhydrous celloidin (Schering's histological grade) in 200 millilitres of acetone. Into this solution was blown distilled water in a very fine jet from a pipette with vigorous stirring of the solution contained in a 500-millilitre beaker. When the mixture became cloudy and a gelatinous precipitate appeared (about 60 millilitres of added water), it was filtered through linen. The filtrate was freed of acetone by bubbling filtered air (cotton wool filter) through it until the Rothera test for acetone gave only a faintly positive result. This required about two hours. After being filtered through linen again the particles were separated by centrifugation (five minutes at 2,500 revolutions per minute). The supernatant fluid was then removed and again subjected to centrifugation to obtain a further yield of particles. This procedure was repeated till no more particles were thrown down. The pooled particles were then suspended in distilled water and adjusted to such a strength that a dilution of 1 in 15 matched a number 7 Burroughs Wellcome opacity tube. This is the stock suspension of collodion particles.

Particles were sensitized before each batch of tests in the following manner. To one millilitre of Kahn antigen (Commonwealth Serum Laboratories) 0·85% saline solution was added according to titre. After the mixture had stood for ten minutes, 0·5 millilitre of stock collodion particles was added to 0·6 millilitre of prepared Kahn antigen. After thorough mixing the tube containing the above was placed in an ice-water mixture for fifteen minutes. Five millilitres of normal saline solution were then added and particles were separated by centrifugation for five minutes at 2,500 revolutions per minute. This washing was repeated twice. Particles were then suspended in sufficient saline solution to match a number 5 Burroughs Wellcome opacity tube. This usually required about 18 millilitres of 0·85% saline solution. The sensitized particles were used within two hours of preparation.

In the test proper serum was inactivated and diluted with saline solution so that the ratio of serum to saline solution was one to four. To 0·3 millilitre of diluted serum an equal volume of sensitized particle suspension was added in a tube with an internal diameter of nine millimetres. The tube was shaken in a rack for thirty seconds, then allowed to stand at room temperature for ten minutes, and finally put in the centrifuge for one minute at 2,000 revolutions per minute. The supernatant

TABLE IIA.

Sera Yielding "+", "++", "+++" or "++++" Positive Reactions.

Type of Response.	Column I. (Progress Patients.)	Column II. (Probably Syphilitic.)	Column III. (Probably not Syphilitic.)	Column IV. (Doubtful.)	Column V. (No Data.)
1. Positive response to one or more of the three tests ..	199 (100%)	72 (100%)	85 (100%)	26 (100%)	44 (100%)
2. Positive response to Wassermann test only ..	169 (85%)	61 (84%)	74 (87%)	21 (81%)	30 (68%)
3. Positive response to Kline test only	164 (82%)	62 (86%)	9 (10%)	10 (38%)	19 (43%)
4. Positive response to Berger test only	172 (86%)	68 (94%)	16 (18%)	12 (46%)	25 (57%)
5. Positive response to Wassermann and/or Kline test	185 (92%)	68 (94%)	76 (89%)	24 (92%)	38 (86%)
6. Positive response to Wassermann and/or Berger test	195 (97%)	70 (97%)	84 (99%)	23 (88%)	39 (88%)
7. Positive response to Kline and/or Berger test ..	182 (91%)	71 (98%)	19 (22%)	15 (57%)	31 (70%)

TABLE IIB.

Sera Yielding "+++" or "++++" Positive Reactions.

Type of Response.	Column I. (Progress Patients.)	Column II. (Probably Syphilitic.)	Column III. (Probably not Syphilitic.)	Column IV. (Doubtful.)	Column V. (No Data.)
8. Positive response to one or more of the three tests	130 (65%)	66 (91%)	10 (11%)	10 (38%)	16 (36%)
9. Positive response to Wassermann test only ..	78 (39%)	56 (77%)	8 (9%)	7 (26%)	5 (11%)
10. Positive response to Kline test only	57 (28%)	42 (59%)	2 (2%)	3 (11%)	1 (2%)
11. Positive response to Berger test only	92 (46%)	59 (82%)	3 (3%)	4 (15%)	9 (21%)
12. Positive response to Wassermann and/or Kline test	92 (46%)	59 (82%)	8 (9%)	8 (30%)	6 (13%)
13. Positive response to Wassermann and/or Berger test	126 (63%)	65 (90%)	11 (12%)	9 (34%)	12 (27%)
14. Positive response to Berger and/or Kline test ..	116 (58%)	64 (89%)	4 (4%)	6 (23%)	10 (22%)

TABLE III.

Estimate of Total Number of Positive Results from Different Tests among Syphilitic Sera on the Two Standards of Positivity Adopted (from Tables IIA and IIB). The Calculated Sensitivity is also Shown.

Wassermann Test.		Kline Test.		Berger Test.	
Positive Result, +, ++, +++, ++++.		*Positive Result*, +, ++, +++, ++++.		*Positive Result*, +, ++, +++, ++++.	
Whole cell defined by Column I, Row 2	169	Whole cell defined by Column I, Row 3 ..	184	Whole cell defined by Column I, Row 4	172
Whole cell defined by Column II, Row 2	61	Whole cell defined by Column II, Row 3	62	Whole cell defined by Column II, Row 4..	68
Half of cell defined by Column IV, Row 2	10	Half of cell defined by Column IV, Row 3..	5	Half of cell defined by Column IV, Row 4..	6
Half of cell defined by Column V, Row 2	15	Half of cell defined by Column V, Row 3..	9	Half of cell defined by Column V, Row 4..	12
	255		240		258
Calculated sensitivity, 83%.		Calculated sensitivity, 78%.		Calculated sensitivity, 84%.	
Positive Result, +++ *or* ++++.		*Positive Result*, +++ *or* ++++.		*Positive Result*, +++ *or* ++++.	
Whole cell defined by Column I, Row 9	78	Whole cell defined by Column I, Row 10	57	Whole cell defined by Column I, Row 11	92
Whole cell defined by Column II, Row 9	56	Whole cell defined by Column II, Row 10	42	Whole cell defined by Column II, Row 11..	59
Half of cell defined by Column IV, Row 9	3	Half of cell defined by Column IV, Row 10	1	Half of cell defined by Column IV, Row 11	2
Half of cell defined by Column V, Row 9	2	Half of cell defined by Column V, Row 10	—	Half of cell defined by Column V, Row 11	4
	139		100		157
Calculated sensitivity, 45%.		Calculated sensitivity, 32%.		Calculated sensitivity, 51%.	

fluid was decanted by quickly inverting the tube, and 0·5 millilitre of saline solution was added. The tubes were tapped and examined for clump formation.

The results were recorded as follows: "–", no clumping—fluid uniformly turbid; "+", small clumps in turbid fluid; "++", small clumps in clear fluid; "+++", medium-sized clumps in clear fluid; "++++", coarse clumps (about three or four) in clear fluid.

Comment on Technique of Berger's Test.

It should be noted that the preparation of stock collodion particles is not difficult, and in any case has to be carried out only infrequently. Care with regard to the force and fineness of the jet of water as well as in the matter of agitation will greatly increase the yield. Furthermore, some samples of celloidin form a much denser suspension of particles than do other samples. In the preparation of the particles Berger removed the acetone by distillation under reduced pressure. This method seems to have objections. It reduces the yield of particles by aggregation, and the suspension appears to last satisfactorily for only six weeks. In the removal of acetone by the aeration technique there is very slight loss by aggregation, and the suspension is stable and satisfactory for at least eight months. In resuspending the particles after centrifugation in the test proper, the saline solution should be gently run down the side of the tube and the deposit disturbed by suitable flipping with the finger. This allows the agglutination to be seen to advantage, when the results are clear-cut and easy to read. Berger gave no scale for recording the strength of the reaction, so that the scale set out above has been adopted arbitrarily.

In actual practice the test can be carried out expeditiously (fifty tests in an hour by one worker and assistant).

Analysis of Result.

In the assessment of the sensitivity and non-specificity rates of various tests for syphilis it is obvious that the figure arrived at will depend upon the class of case used in the investigation and upon the degree of reaction accepted as positive. An analysis of the findings with regard to these points is now presented.

The series analysed was accumulated between October, 1945, and December, 1946. All specimens of serum examined have been included except those "positive" specimens which were used again as "positive" controls. Cerebro-spinal fluid has been omitted from consideration as the number of specimens was not great.

The following tabulation indicates the number of specimens of serum yielding reactions to any degree positive to one or more of the tests.

Number of specimens giving results positive to any degree by one or more tests	426
Number of specimens giving negative results to all tests	1,969
Total	2,395

The following shows the number of positive reactions to the three tests separately:

Number of results positive to any degree by one or more methods	426
Number of results positive to any degree by Wassermann test alone	355
Number of results positive to any degree by Kline test alone	204
Number of results positive to any degree by Berger test alone	303

A difference in results obtained by the three tests is clearly indicated by this second set of figures. To investigate this difference further the positively reacting specimens of serum were subdivided into the following five classes.

Class I: Serum of "Progress" Patients.

"Progress" patients had been accepted for treatment at the syphilis clinic and are considered to be practically certainly syphilitic. The results of the tests on such

TABLE IV.

Estimate of Total Number of Positive Results from Different Tests among Non-Syphilitic Sera on the Two Standards of Positivity Adopted (from Tables IIA and IIB). The Calculated Non-Specificity is also Shown.

Wassermann Test.		Kline Test.		Berger Test.	
Positive Result, +, ++, +++ *or* ++++.		*Positive Result*, +, ++, +++ *or* ++++.		*Positive Result*, +, ++, +++ *or* ++++	
Whole cell defined by Column III, Row 2 ..	74	Whole cell defined by Column III, Row 3 ..	9	Whole cell defined by Column III, Row 4 ..	16
Half of cell defined by Column IV, Row 2 ..	10	Half of cell defined by Column IV, Row 3 ..	5	Half of cell defined by Column IV, Row 4 ..	6
Half of cell defined by Column V, Row 2 ..	15	Half of cell defined by Column V, Row 3 ..	9	Half of cell defined by Column V, Row 4 ..	12
	99		23		34
Calculated non-specificity, 4·7%.		Calculated non-specificity, 1·1%.		Calculated non-specificity, 1·6%.	
Positive Result, +++ *or* ++++.		*Positive Result*, +++ *or* ++++.		*Positive Result*, +++ *or* ++++.	
Whole cell defined by Column III, Row 9 ..	8	Whole cell defined by Column III, Row 10 ..	2	Whole cell defined by Column III, Row 11 ..	3
Half of cell defined by Column IV, Row 9 ..	3	Half of cell defined by Column IV, Row 10	1	Half of cell defined by Column IV, Row 11	2
Half of cell defined by Column V, Row 9 ..	2	Half of cell defined by Column V, Row 10	—	Half of cell defined by Column V, Row 11	4
	13		3		9
Calculated non-specificity, 0·62%.		Calculated non-specificity, 0·14%.		Calculated non-specificity, 0·43%.	

TABLE V.

Test.	Figures Obtained by Berger.		Figures Obtained at Newcastle.			
			Lower Standard of Positivity.		Higher Standard of Positivity.	
	Sensitivity.	Non-specificity.	Sensitivity.	Non-specificity.	Sensitivity.	Non-specificity.
Wassermann ..	67·0%	0·2%	83·0%	4·7%	45·0%	0·62%
Kahn	66·0%	0·1%	—	—	—	—
Kline	—	—	78·0%	1·1%	32·0%	0·14%
Berger	100·0%	1·9%	84·0%	1·6%	51·0%	0·43%

specimens of serum indicate the sensitivities of the tests on the serum of treated patients.

Class II: Serum of Patients Probably Syphilitic.

In the Class II cases a typically syphilitic lesion was recorded in the notes—for example, lightning pains, punched-out ulcers, aortic aneurysm, interstitial keratitis, birth of a child with a syphilitic lesion. Besides the above-mentioned condition, it was also required that no other condition known to cause "false positive" reactions should be present. Into Class II was also admitted the serum of patients reacting both to the Wassermann test and to the Kline test (no less than "+++"), if no other data were available. This admission was considered justified because general usage has established the value of these two tests and the present object was to review the Berger test suspiciously rather than the Wassermann and Kline tests. This class is the index of the usefulness of the three tests in diagnosis.

Class III: Serum of Patients Probably Not Syphilitic.

In the Class III cases no typically syphilitic lesion was noted, but there was record of some condition that may have been expected to produce a "false positive" reaction (usually only a "partial positive"). As examples of such conditions may be cited carcinoma of the œsophagus, carcinoma of the stomach, pyrexia of unknown origin, typhus fever, prostatitis. As a complementary proviso it was required that no known syphilitic lesion should be present. Also admitted to this category was serum which no longer reacted on reexamination within a few weeks, whether a provocative dose of arsenical drug had or had not been given to the patient. This class is of such a nature as to indicate the non-specificity of the test.

Class IV: Serum of Patients Doubtfully Syphilitic.

In the Class IV cases one or other of the complementary conditions of Classes II and III were absent, or the conditions were in opposition.

Class V: Serum from Patients without Information.

Many of the Class V patients were service personnel and some were seamen temporarily in port. Thus there is a likelihood that some were syphilitic, perhaps under treatment, but it is possible that some had malaria and that their serum may have given "false positive" reactions.

Discussion.

Both the last two classes are of only limited value in the assessment of results.

Table I shows the distribution of cases in these categories.

Tables IIA and IIB show the number of positive reactions within these categories with regard to the tests separately and with regard to the tests in various groups. In Table IIA, a "+", "++", "+++" or "++++" reaction is regarded as positive, whilst in Table IIB only a "+++" or "++++" reaction is regarded as positive. In every instance the number of positive reactions is shown as a percentage in parentheses for ready comparison.

Rows 2, 3 and 4 in column I indicate that the Berger and Wassermann tests are about equal in sensitivity, and perhaps slightly more sensitive than the Kline test in estimating the progress of treated patients. Rows 9, 10 and 11 in the same column show that if a more rigid standard of positivity is adopted the sensitivities vary to a greater extent, and that the Berger test leads, followed by the Wassermann and then the Kline. Although the Berger test shows the greatest sensitivity and the Kline the least sensitivity (rows 3 and 4 in column I), it will be noted that the figure derived by accepting as positive a reaction to the Berger or Kline test, or to both (row 7 in column I), is greater than that for the Berger test alone. This is a reflection of the fact that from most specimens of serum that react positive results are obtained by both methods, but sometimes by only one or other. That is to say, besides differences in the sensitivity of the methods there is some qualitative difference as well. Further instances can be found on comparing similar groups of sensitivities throughout the table.

Column II indicates that for diagnostic purposes the order of sensitivities is Berger test, Kline test and Wassermann test. Again, higher figures are noted for the various combinations. As before, there is some loss in sensitivity, and the order of sensitivity becomes Berger test, Wassermann test, Kline test when the more rigid standard of positivity of Table IIB is adopted.

Column III indicates the likelihood of false reactions. The Wassermann test has by far the greatest non-specificity rate. These figures are greatly reduced by adoption of the higher standard of positivity.

To make a comparison with Berger's conclusions, sensitivity and non-specificity have been computed after the manner of Berger. The total numbers of syphilitic sera have been calculated by taking the sum indicated in the following figures: all of Class I, 199; all of Class II, 72; half of Class IV, 13; half of Class V, 22; total, 306.

Table III shows the estimation of the total of positive Wassermann, Kline and Berger reactions among the sera of syphilitics. The figures are set out on the two standards of positivity previously adopted. The sensitivities are also expressed as percentages of total syphilitic sera as estimated in the preceding paragraph.

To arrive at the non-specificity rate the total of non-syphilitic sera was estimated as follows: sera giving negative results to all tests, 1,969; all of Class III, 85; half of Class IV, 13; half of Class V, 22; total, 2,089.

The total number of sera giving "falsely positive" reactions amongst non-syphilitic sera in response to the difference tests is estimated as in Table IV. Figures are given on the basis of the two standards adopted, and non-specificities are shown as percentages.

Table V gives a comparison between the figures obtained by Berger and those obtained at Newcastle. As was indicated earlier, it is considered that the actual figures obtained will depend upon the class of case under investigation, and for this reason it is thought that a study of the relative sensitivity and non-specificity rates in Classes I, II and III as contained in Table II gives the best indication of the relative merits of the tests.

Conclusion.

The present experience indicates that the Berger test is valuable in the diagnosis and control of syphilis and is worthy of use in conjunction with other serological tests. Like the other two, it produces "false positive" reactions at times and does not always produce positive reactions with the serum of syphilitics. However, in these respects it does not coincide exactly with the Wassermann or Kline

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test, so that the use of as many tests as practicable is desirable. The facility of carrying out the Berger test commends it for general use.

Acknowledgements.

For clinical data in certain of the cases I am indebted to Dr. A. B. K. Watkins, Dr. F. J. Collins and Dr. Idris Morgan. Dr. G. H. Hair has assisted with data and advice concerning the likelihood of some ophthalmic conditions being syphilitic in origin. The laboratory procedures of the tests have been carried out by Mr. H. H. King.

Reference.

(1) F. M. Berger: "An Agglutination Test for the Serological Diagnosis of Syphilis", *The Journal of Pathology and Bacteriology*, Volume LV, July, 1943, page 363.

THE HYPOPROTHROMBINÆMIC EFFECT OF 3,3'ETHYLIDENE-BIS-4-HYDROXYCOUMARIN (E.D.C.): AN EXPERIMENTAL AND CLINICAL STUDY.

By P. FANTL and MARGARET H. NANCE,[1]

From the Baker Medical Research Institute, Alfred Hospital, Prahran, Melbourne.

THE prophylaxis against and the treatment of thromboembolism by drugs interfering with blood coagulation assumes that there is a primary relationship between thrombus formation and the clotting system. Evidence has been furnished that substances inhibiting the essential components of the coagulation system will prevent thrombus formation in laboratory animals.[1][2] Although a number of compounds capable of delaying blood coagulation are available, it appears that only two have found practical application in the prevention and treatment of thrombotic conditions. These are heparin and 3,3'methylene-bis-4-hydroxycoumarin or "Dicumarol". Heparin affects the whole blood coagulation time by inhibiting thrombin formation and thrombin action. It has the advantage of prompt action. The effect, however, is of short duration, necessitating frequent parenteral injections. On the other hand, "Dicumarol" acts after oral as well as parenteral administration by reducing prothrombin activity, and when applied in therapeutic doses has no effect on the coagulation time of whole blood. The latter is governed by the concentration of the essential factors involved. It appears that normal blood has a low concentration of thromboplastin, which therefore is the limiting factor. Its amount is sufficient to convert only a fraction of prothrombin. Theoretically, therefore, only severe hypoprothrombinæmia could be effective in preventing thrombus formation; but it has been shown that prothrombin concentrations of approximately 25% of the normal are adequate, and at such a concentration whole blood coagulation time is not altered. This indicates that other factors apart from hypoprothrombinæmia are operative in the action of dicoumarin drugs. No influence on the number of circulating platelets has been observed during "Dicumarol" treatment; but according to H. P. Wright[3] the adhesiveness of the platelets is lessened, and this may be a contributory factor in the therapeutic action. The drawbacks of the drug are its delayed action and the fact that, according to the experience of Barker *et alii*,[4] the recovery from the induced hypoprothrombinæmia may take from two to ten days after discontinuance of its administration. It was this latter disadvantage which led to the study of compounds which gave a shorter recovery period. It has been reported that 3,3'ethylidene-bis-4-hydroxycoumarin (E.D.C.) has such an advantage.[5]

Additional animal experiments have been carried out, larger doses of E.D.C. being used. Rabbits weighing between 1·4 and 2·0 kilograms were used. Those in groups I to III received 30 milligrammes of E.D.C. suspended in 2·0 millilitres of water by stomach tube on three successive days. Animals in groups A to C received 20 milligrammes of E.D.C. orally. The prothrombin estimations were carried out on 100% plasma and plasma diluted to 12·5% with isotonic saline solution according to the techniques of Quick[6] and Campbell *et alii*,[10] 3% rabbit brain suspension and a 0·01 molar solution of calcium chloride being used. Results are set out in Table I.

Because of a variation in the potency of the thromboplastin preparation, normal controls were included for each reading. In this series undiluted normal rabbit plasma gave clotting times between six and seven seconds, while the 12·5% plasma clotted in twelve to fifteen seconds. It is apparent from the second readings that all animals had suffered a severe reduction in the plasma prothrombin level. The third reading indicated that four out of six animals had completely recovered when judged by the results obtained with diluted plasma, and the remaining two had prothrombin levels of over 50% of the premedication value, so that in all these animals there was now no danger of hæmorrhage. The animals received amounts of E.D.C. per kilogram of body weight in three days corresponding to the total dose given to human beings over six to ten days.

In order to find out the extent of liver damage produced by toxic doses of E.D.C., guinea-pigs were given intraperitoneal injections of 75 to 100 milligrammes per kilogram of body weight on three consecutive days and were sacrificed twenty-four hours after the last dose (Table II). According to the prothrombin times, all the treated animals showed an almost complete deficiency twenty-four hours after the last dose, when judged by the method using a 0·01 molar solution of calcium chloride for recalcification.

In agreement with observations made by Jaques and Dunlop[7] with "Dicumarol" in dogs, the prothrombin times were found to be much reduced when a higher calcium concentration (0·025 molar solution of calcium chloride) was used (see column 2, Table II). In spite of the severe prothrombin deficiency, only two out of the twelve animals so treated died from internal hæmorrhages. The estimation of prothrombin time in such severe hypoprothrom-

[1] Working under a full-time grant from the National Health and Medical Research Council.

TABLE I.

Reaction of Rabbits to Oral Administration of E.D.C. Clotting Times are given in Seconds.

	Initial Values.		Two Hours after E.D.C. Third Administration.		Forty-eight Hours after Last Dose.		Fibrinogen. (Milligrammes *per Centum*.)		
	100·0%	12·5%	100·0%	12·5%	100·0%	12·5%	Before Treatment.	After Treatment.	Increase.
1.. ..	6·0	15·9	34·0	49·0	6·2	11·2	—	—	—
2.. ..	6·2	12·4	27·0	39·0	7·6	14·7	—	—	—
3.. ..	6·3	13·2	19·0	33·0	8·0	16·7	—	—	—
Average	6·2	13·8	27·0	40·3	7·3	14·2	—	—	—
A ..	7·0	13·5	9·0	26·0	8·2	16·2	254	330	+30%
B ..	7·0	13·0	11·0	22·0	7·2	12·0	—	—	—
C ..	6·5	14·5	10·0	22·0	7·0	14·2	252	485	+90%
Average	6·8	13·7	10·0	23·0	7·5	14·1	—	—	—

binæmia in this species is apparently not an absolute index, because the plasma coagulation times, as judged by simple recalcification without any additional thromboplastin, are much shorter than the corresponding prothrombin times (see column 3, Table II). The reason for the inhibiting action of homologous brain extract may be due to the presence of anticoagulant substances in brain in addition to the coagulation-promoting thromboplastin. Similar phenomena have been observed to follow the administration of "Dicumarol" to humans in cases of extreme prothrombin deficiency.[6] It is probable that in such instances Russell viper venom activated by lecithin will give a better indication of the degree of hypoprothrombinæmia as is suggested by the results shown in column 4, Table II. Further evidence of toxic effects of the drug is seen in the alteration of fibrinogen concentration in plasma, which in the average amounted to an increase of 16%.

TABLE II.

Treatment of Guinea-Pigs with Toxic Doses of E.D.C. Coagulation Times are given in Seconds.

	Prothrombin Time. (Guinea-pig Brain.)		Coagulation Time of Plasma Using 0·025 M Calcium Chloride.	Prothrombin Time Using Russell Viper Venom *plus* Lecithin.	Fibrinogen. (Milligrammes *per Centum*.)
	0·01 M Calcium Chloride.	0·025 M Calcium Chloride.			
	(1)	(2)	(3)	(4)	(5)
A	∞	∞	—	∞	
B	540	210	140	60	513
C	5,400	690	—	120	515
X	∞	510	112	57	465
Y	270	180	105	49	440
Z	600	180	115	50	555
Control	20	20–24	30–46	10–15	350–440

The livers were removed and examined by Dr. W. E. King, who reported no liver damage apart from congestion and hyperæmia.

The Effect of E.D.C. on Humans.

The purpose of this treatment is to produce and maintain prothrombin levels low enough to prevent thrombus formation and extension without the risk of hæmorrhages. Most workers who use "Dicumarol" agree that this can be achieved by a prothrombin level of approximately 30% of normal. Our evidence for the efficacy of E.D.C. has been derived from experiments carried out on 45 patients. No effect on the prothrombin level was observed in the case of three patients who received a single dose of 0·5 gramme. With the administration of 0·5 gramme on two successive days, of six patients so treated, five reacted and one was resistant; hypoprothrombinæmia was observed between twenty-four and forty-eight hours after administration of the first dose. Thirteen patients have been treated for a period of three days, and of these one was resistant. The results are as set out in Table III.

Further, 23 patients have been treated with two doses of 0·5 gramme and doses varying from 0·35 to 0·1 gramme daily for periods up to three weeks. It was possible to reduce the prothrombin level in 15 cases to below 50%, although great variations in response were observed. In all, five subjects were found to be resistant, including one who received three daily doses of 0·5 gramme. No attempt was made to overcome this resistance by increasing the dosage. It seems that extremely wide variations occur in the response to the drug, but this fact has no apparent relation to age, sex, pathological state[1] or other treatment. This great variation in response makes it essential to carry out frequent prothrombin estimations. These have been made either in venous or in capillary blood after it had been established that the two techniques gave essentially identical results. The dosage of E.D.C. has been adjusted to the prothrombin level. On two occasions it was desired to subject patients to two courses of E.D.C. treatment, and one of these will be described in more detail.

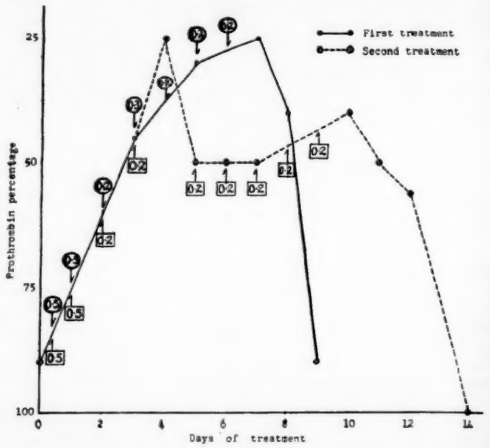

FIGURE I.

Dosage of E.D.C. in grammes given during first treatment indicated by figures in circles. Dosage of E.D.C. in grammes given during second treatment indicated by figures in squares.

The patient was a married woman on whom laparotomy and transverse colostomy were performed by Dr. L. Ball, and eight days later the patient developed bilateral pulmonary embolism with no evidence of thrombosis. E.D.C. treatment was started at once and continued for six days. Two days later the prothrombin time was normal, and excision of a carcinoma of the sigmoid colon was performed.

[1] No patients with deficient liver or kidney function were treated.

TABLE III.

Influence of E.D.C. on Prothrombin Activity during Three Days' Treatment; 0·5 Gramme was given on the First Two Days and 0·2 Gramme on the Third Day. Figures indicate Prothrombin Percentage after Discontinuance of the Drug.

Patient.	Twenty-four Hours.	Forty-eight Hours.	Seventy-two Hours.	Age.	Disease.
Ell.	25	100	—	63	Osteomyelitis.
Pa.	20	59	62	14	Rheumatic fever.
Hi.	0	30	40	65	Thrombosis of left arm.
Br.	20	—	100	52	Thrombosis of leg vein and diabetes.
Eg. I	—	50	75	60	Pulmonary embolism following femoral thrombosis.
Eg. II ..	35	60	75	60	
Du.	10	—	80	61	Arteriosclerosis and myocardial failure.
Fa.	50	—	100	67	Hypertension and senile dementia.
Mi.	40	—	100	39	Fractured patella (excised).
Fl.	30	—	100	40	Convalescence after herniotomy.
Ca.	10	—	100	19	Fractured tibia and fibula.
Da.	13	—	Patient left hospital.	78	Arteriosclerosis and myocardial failure.

Five days after the second operation the patient developed thrombosis of the right calf and E.D.C. treatment was again given for nine days. About three weeks later the colostomy was closed.

None of the patients complained of ill effects, and apparently no impairment of liver or kidney function resulted.

Fibrinogen estimations before and after recovery from the hypoprothrombinæmia indicated that in patients who gave a positive response to E.D.C., the fibrinogen production was also influenced, although no correlation between severity of hypoprothrombinæmia and alteration of fibrinogen levels could be observed. Since the patients were recovering from operations the fibrinogen levels may have been influenced by this factor (Table IV).

TABLE IV.

Influence of E.D.C. on Fibrinogen Concentration. Figures are Calculated in Milligrammes per Centum of Fibrinogen in Fresh Plasma.

Patient.	Before Treatment.	After Treatment.	Total Dosage of E.D.C. in Grammes.	Difference *per Centum.*	Minimal Prothrombin Level *per Centum.*
Ba. ..	402	315	1·6	−21	50
Pe. ..	290	295	1·6	0	100
Du. ..	408	545	1·35	+33	10
Fa. ..	312	343	1·35	+10	50
Mi. ..	388	366	1·35	−7	40
Fi. ..	379	335	1·35	−12	30
Ca. ..	309	360	1·35	+20	10
Br. ..	348	300	1·6	−14	15
McN. ..	220	173	1·6	−22	25

Protective Influence of Vitamin K Active Substances.

Although there arose no need to treat hæmorrhages during E.D.C. treatment in the present series, it was felt that in an emergency countermeasures should be available. From the experience of workers using "Dicumarol" it appears that transfusion of fresh blood or large doses of a vitamin *K* preparation are effective. Rabbits received 50 milligrammes of 2-methyl-1,4-naphthohydroquinone sodium monophosphate[1] in two millilitres of sterile saline solution intravenously on three successive days. Half an hour after the injection they were given by stomach tube a suspension of 25 to 30 milligrammes of E.D.C. in two millilitres of water. Control animals received similar amounts of E.D.C. only.

Four months later the animals which served as controls in the previous experiment were treated with vitamin *K* and E.D.C., and the other group were used as controls. Results essentially similar to those of the previous experiment were obtained. The experiments indicated that the vitamin *K* preparation was of value in counteracting the effect of E.D.C.

The Significance of Coagulation Anomalies in Thrombotic States.

The insidious onset of thrombotic conditions and the unexpected appearance of pulmonary embolism without premonitory symptoms make it desirable to have a reliable biochemical test for the selection of patients requiring treatment. There is no lack of suggestions, and some experimental evidence seems to indicate that the biochemistry of the blood may give a clue. In normal persons a slight tendency for lower extremity blood to clot faster than upper extremity blood has been detected by Shafiroff *et alii*.[9] This phenomenon was markedly exaggerated in the blood from thrombophlebitic limbs. All the proposed tests centre round the assumption that increased coagulability of blood is a predisposing and essential factor in the causation of intravascular thrombosis. We have devoted some attention to the diagnostic value of several tests.

A perusal of the literature pertaining to the connexion between blood coagulation time and tendency to thrombosis indicates that all three theoretically possible results have been observed. Some authors find a connexion, others deny that an increase of the coagulation tendency bears any relationship, and the third group believes that the changes do not follow any law. It should be pointed out that the estimation of whole blood coagulation time is of value only when carried out under rigidly standardized conditions. Dale and Laidlaw[10] have already drawn attention to the necessity for this, but it appears that not all workers in this field heeded their precautions. With a standard technique it will be found that the coagulation time is constant for the normal individual independently of the time of day and of meals—a fact which has been confirmed again by Bergquist.[11] In spite of this, a recent statement that the blood coagulation time of any person varies from hour to hour appears in the literature.[12] We have carried out estimations of whole blood coagulation times in venous and capillary blood from 32 patients prior to and during E.D.C. treatment. The technique consisted of recalcification of 0·1 or 0·04 millilitre of oxalated whole blood with an equal volume of a 0·025 molar calcium chloride solution at 37·5° C. Under these conditions normal blood coagulated in from 70 to 100 seconds. No significant difference was observed on successive days, and a reduction in prothrombin activity of 75% did not alter the whole blood coagulation time. Estimations by the Lee-White technique[13] on venous blood of two patients, in whom even minor surgical intervention in the past had led to attacks of embolism, did not show any shortening in whole blood coagulation time.

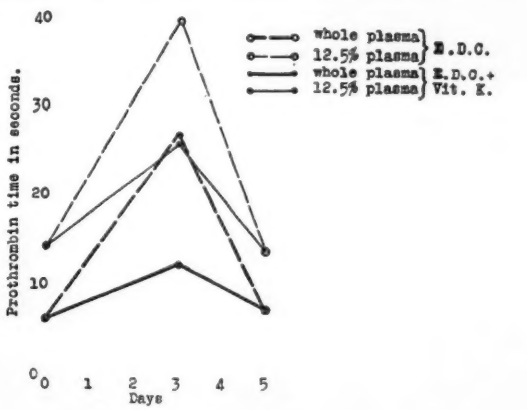

FIGURE II.

The points of the curve indicate prothrombin times at the following intervals: no days, initial level; three days, 1·5 hours after third treatment; five days, forty-eight hours after discontinuance of treatment.

Bergquist[11] finds an acceleration of whole blood coagulation time following the onset of coronary thrombosis; but according to him the first attack is not initiated by accelerated coagulation. This author states:

> As regards the coagulation time it has been found to be shorter than normal in certain cases of thrombosis, but this is not a regular occurrence, so that this blood change has no diagnostic value. . . .

Another test which has been proposed by Shapiro[14] rests on the assumption that a greater prothrombin activity is the predisposing factor for thrombus formation. The estimation is carried out in diluted plasma and an established hyperprothrombinæmia is considered a premonitory sign of thromboembolism. Brambel and Loker[15] found increased prothrombin activity in phlebitis, following operative surgical trauma, and during childbirth as a regular phenomenon. We performed the test on several occasions and greater prothrombin activity was observed in late pregnancy and in two cases of thrombophlebitis. However, it was also seen in two cases of hypertension in which there was no history of thrombosis, and activity was normal in a case of severe thrombophlebitis and postoperatively in two cases in which there was a history of pulmonary embolism following minor surgical interference. In addition, greater prothrombin activity was observed in

[1] The vitamin *K* preparation was supplied by Nicholas, Proprietary, Limited.

two "bleeders", one of whom had a greatly delayed coagulation time. From these observations it is apparent that decreased prothrombin time as shown in diluted plasma may be of significance for the diagnosis of thrombosis only in subjects with normal or reduced whole blood coagulation time. Thus it appears that the majority of persons either threatened by or suffering from thrombosis may show a shortened coagulation time in the one or the other test. A percentage only will develop pulmonary embolism, which makes any of the above tests of doubtful value for diagnostic purposes.

Other tests indicating hypercoagulability in thrombotic states, heparin being used *in vivo* (De Takats[16]) and also *in vitro* (Waugh and Ruddick[17]), and finally a thrombin stability test (Lenggenhager[18]) have been advocated; but without experience we are not in a position to discuss their value.

Summary.

Experimental evidence is presented demonstrating the efficacy of 3,3'ethylidene-bis-4-hydroxycoumarin as a drug for reducing prothrombin activity in humans. The response varies from nil to severe hypoprothrombinæmia. Recovery after termination of E.D.C. treatment appears to be shorter than after "Dicumarol" treatment. When E.D.C. was used in therapeutic dosages, no toxic effects, except a change in fibrinogen level, were encountered.

Acknowledgements.

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AN OUTBREAK OF DYSENTERY CAUSED BY SHIGELLA SCHMITZI.

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ALTHOUGH sporadic infections due to *Shigella schmitzi* have occurred in all the larger epidemics of bacillary dysentery reported during the war years, we are unaware of any reference to an outbreak in which this organism was the sole ætiological agent. The present paper deals with 51 cases at an Australian general hospital over a period of three months, in which the causative organism was isolated and identified as *Shigella schmitzi.*

The first outbreak of this nature occurred in a Rumanian prisoner-of-war camp in the first World War,[1] and was reported by Schmitz. Since then further series of cases have been published in England[2] and in South America;[3] but outbreaks confined to this type of organism have been rare.

The ætiological factors in the outbreak here described differed little from those usually associated with dysentery in tropical areas, where the exigencies of service conditions often caused temporary overcrowding of troops into areas not fully prepared.

In the present instance the sudden arrival at an island staging area of a whole division destined for the Borneo campaign was the exciting factor. The outbreak began quietly with eleven cases in the first month, but quickly gathered momentum in the second month, when 35 cases occurred. There were eleven cases in the first week, thirteen in the second week, four in the third week, and seven in the last ten days of the second month. During the third month only five patients were admitted to hospital. The decline in incidence was related to the determined efforts made by the camp authorities to remove all potential sources of infection. The measures adopted were designed to eliminate all fly-breeding grounds, to make flyproof all latrines and kitchens, and to prohibit from food handling any soldier complaining of even the slightest looseness of the bowels.

Clinical Features.

In general the clinical features of this outbreak did not differ greatly from those seen in previous epidemics, except for the occurrence of a small number of cases (four) in which the general features of an infective process were apparent, but no local features.

For the purpose of description the cases have been divided into three groups. In the main group, most, if not all, of the signs and symptoms common to bacillary dysentery were present. On the other hand, at the onset of the infection, the other two groups presented a problem in diagnosis, and the patients were admitted to general medical wards for investigation.

Group I.

The patients in the first group numbered 38, and showed what may best be described as the classical symptoms of dysentery; this group will be referred to as the gastro-enteritic type. As the presenting symptom, all patients gave a history of diarrhœa of varying severity. In the majority (27 cases) this was the passage of about ten or more watery stools in the preceding twelve hours. Associated symptoms included vomiting in 22 cases, generalized aches and pains in 25 cases, and abdominal colic and cramp in 38 cases. Rigors were present in 15 cases.

On examination of the patients, the most noticeable finding was the wide variation in general appearance. Out

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of 38 patients in this group, 18 showed very little toxæmia and did not appear ill at all. On the other hand, 20 patients showed some pallor, slight dehydration, an exhausted, somewhat anxious expression, a temperature over 103° F., and a pulse rate varying between 92 and 110 per minute. A typical example of this group is the following.

An officer, A.E., aged forty-eight years, with no history of previous ill health, was well until the morning of his admission to hospital, when he felt off colour without any definite symptoms. Three hours later he noticed the onset of colicky lower abdominal pain with the passage of frequent stools (eleven in eight hours). He stated that slime was present in his stools, but no blood was seen. The diarrhœa was followed by nausea, vomiting and severe headache.

Examination revealed some facial pallor, but no pronounced distress. The temperature was 103·6° F. and the pulse rate 92 per minute, and the respirations numbered 22 per minute. Clinically the throat, heart, lungs and nervous system appeared normal. Examination of the abdomen revealed some tenderness over the large bowel, particularly the descending colon; otherwise no abnormality was detected. A stool was found to be fluid and to contain very little mucus. Microscopic examination revealed an indefinite exudate. Culture of the fæces produced a growth of *Shigella schmitzi*.

The patient was treated with sulphaguanidine in the usual dosage (that is, six grammes initially, followed by three grammes every four hours until the stools were reduced to two or three per day, and then by three grammes three times a day for three days). Within twenty-four hours the temperature and pulse rate had fallen to normal. Sigmoidoscopic examination failed to disclose any abnormality, and the patient was discharged to his unit.

Group II.

Although it occurred only in small numbers, the second type of case exemplified the difficulty of diagnosis of dysentery in tropical areas. The four patients comprising this group were all admitted to general medical wards with the diagnosis of pyrexia of uncertain origin. None of them gave a history which suggested a bowel infection as the primary cause. Indeed, in one case the diagnosis of meningitis had been considered by the regimental medical officer and the duty medical officer.

All four patients presented with headache and rigors associated with vomiting. None had passed more than two stools in the preceding twenty-four hours. After their admission to hospital, all four patients passed one or two liquid, offensive stools, and from these a culture of *Shigella schmitzi* was obtained. Repeated examinations for malaria parasites gave negative results. All the patients were showing definite clinical improvement by the time the causal organism had been isolated.

The following is a typical clinical history.

Gunner W., aged twenty-one years, complained of severe headache, which had commenced thirty-six hours previously, and had reached its maximum intensity four hours prior to his admission to hospital. Subsequently it diminished in severity. The headache was mainly frontal and behind the eyes, and was aggravated by movement or coughing. He had shivered and vomited twice during the day prior to admission. For the preceding three weeks he had had a persistent cough and cold. In the past twenty-four hours his bowels had been open twice, with the passage of formed stools. Micturition was normal.

Examination disclosed the patient to be a flushed young man with an anxious expression. His temperature was 104° F., his pulse rate was 130 per minute, and his respirations numbered 28 per minute. The cardio-vascular, respiratory and alimentary systems appeared normal. Some neck rigidity was present.

A tentative diagnosis of a respiratory infection was made and the patient was placed under observation. Next day he passed one loose, brown stool, and another on the following day. When he first complained of abdominal pains forty-eight hours after his admission to hospital, the temperature and pulse rate had returned to normal.

Examination of the fæces revealed a liquid brown stool with flecks of mucus. Microscopic examination revealed an indefinite exudate. However, culture produced a growth of *Shigella schmitzi*. Sigmoidoscopy at this stage disclosed some hyperæmia of the mucosa, but no ulceration. The patient made an uneventful recovery under routine sulphaguanidine therapy. At the conclusion of treatment sigmoidoscopy was repeated and the bowel was normal. After two weeks in hospital he was discharged to a convalescent depot.

Group III.

The third group comprised the mild cases which were probably responsible for keeping the epidemic going. These patients presented with mild abdominal symptoms and some diarrhœa, the latter symptom emerging only on closer questioning. There is little doubt that such patients can be overlooked, and if they are not treated as infective, they are a menace under active service conditions. There were few symptoms and no evidence of any toxæmia. Only five such patients were examined, but it seems likely that a number of the men treated with sulphaguanidine in their lines would have fallen into this category.

The following is a typical clinical history.

Private F.C., aged twenty-one years, was admitted to hospital with a history of mild colicky abdominal pains, of six hours' duration. During this time his bowels had been open twice, but only the second motion had been loose. He did not feel ill and he gave no history of headache, vomiting, nausea or rigors.

Examination showed the patient to be healthy looking, with a normal temperature and pulse rate. No physical abnormality was detected; but a stool passed in the ward was liquid and brown and yielded a positive result on culture.

Sigmoidoscopy revealed a normal-looking bowel. The patient made an uneventful recovery with sulphaguanidine treatment.

Treatment.

The patients were isolated in a fly-proofed "infectious" ward with all the usual precautions. After diagnosis, treatment was carried out with the routine army course of sulphaguanidine. Copious fluids were given orally; parenteral administration was not found to be necessary.

Sigmoidoscopy was a routine procedure in all cases, and if any abnormal findings were discovered the examination was repeated prior to the patient's discharge from hospital. In this series ulceration was seen once; one patient had a small ulcer in the rectum. In 36 cases the sigmoidoscopic findings were normal, while in 14 hyperæmia was observed.

Laboratory Procedures.

During each day all specimens of fæces for cultural examination were brought to the laboratory in the bed pan as soon as possible after they had been passed. A search was made for mucus, and when found it was washed once in saline solution to free it from gross fæcal material, and seeded directly onto desoxycholate-citrate agar plates, into tetrathionate broth and into brilliant green enrichment medium. In addition it was examined as a wet preparation under a cover slip for the type of cell present. The type of exudate was classified into "bacillary", "indefinite" or "nil", according to routine army laboratory procedure. In thirty of these cases a typical bacillary exudate was present, in sixteen the exudate was classed as indefinite, while in six specimens from which the pathogen was recovered, no exudate was present.

The tetrathionate broth and brilliant green enrichment broth, prepared according to the formula given by Hynes,[1] were inoculated with mucus or with several loopfuls of fæcal material, and incubated at 37° C. overnight. On the following morning the cultures were plated on desoxycholate-citrate agar. After a further twenty-four hours' incubation at 37° C., the plates were examined for non-lactose-fermenting colonies. The use of tetrathionate broth and brilliant green enrichment medium was designed to identify the gastro-enteric type of Salmonella infection, and did not assist in the isolation of dysentery bacilli; in fact, such organisms were suppressed by these media. The desoxycholate-citrate agar plate, inoculated directly with washed mucus, was incubated overnight at 37° C., examined next morning for non-lactose-fermenting colonies, and then returned to the incubator for a further twenty-four hours. Experience had shown that *Shigella shigæ* often produced minute colonies that might be missed after twenty-four hours, but became obvious after forty-eight hours' incubation at 37° C. on desoxycholate-citrate agar.

XUM

During the night specimens for cultural examination were collected by the ward staff and placed in 30% glycerol and saline solution buffered at pH 8·0, in tetrathionate broth and in brilliant green broth. Whenever possible a further fresh specimen was sent to the laboratory the next morning for examination as described above.

At least two examples of each type of non-lactose-fermenting colony were picked from each plate and seeded into Kligler's medium, made up in small tubes measuring three inches by one-quarter of an inch, and having a short slope and a butt of about one inch, as recommended by Ferris and Fortune.[5] The Kligler's medium was incubated overnight for a minimum period of eighteen hours at 37° C., and then those cultures showing reactions typical of the dysentery or typhoid-paratyphoid group were subjected to slide agglutination tests. Commonwealth Serum Laboratories agglutinating antisera were available, and cultures showing neither gas formation nor blackening in Kligler's medium were tested with the following antisera: pooled *Shigella flexneri* I, II and III, and pooled *Shigella flexneri* IV, V and VI, *Shigella shigæ*, *Shigella schmitzi*, pooled *Shigella boyd* I, II and III, *Shigella sonne*, *Shigella boyd* P274, and D19 antisera. When gas or blackening, or both, were present in Kligler's medium, a slide agglutination test was performed with polyvalent Salmonella antiserum.

In the cases described here a provisional diagnosis of infection with Schmitz's bacillus was given when a non-lactose-fermenting colony from the desoxycholate-citrate agar plate produced a red slope with yellow butt and no evidence of gas or blackening, and when agglutination occurred specifically with *Shigella schmitzi* antiserum. The diagnosis was confirmed by showing that the organism isolated was a Gram-negative, non-motile bacillus, producing indole, and fermenting glucose but not mannitol, lactose or sucrose. Motility tests were performed on four to six hour peptone water cultures. Fermentation tests were carried out in peptone water containing 0·5% of the test carbohydrate and 1% of Andrade's indicator, the tubes being incubated at 37° C. for five days. Tests for indole were made in five-day-old peptone water cultures. The majority of the strains isolated agglutinated readily when tested from the Kligler's medium, but a few failed to show agglutination with any of the dysentery antisera until they were grown on nutrient agar and tested from this medium. Then they agglutinated readily in *Shigella schmitzi* antiserum. With regard to their colonial characteristics on desoxycholate-citrate agar and Kligler's medium, and to their fermentation reactions, such strains appeared in no other way different from the remainder. This would seem to indicate that while a positive response to the agglutination test may be accepted with confidence, failure to agglutinate from Kligler's medium should be further investigated by subculture onto nutrient agar and by retesting from this medium. Because the occurrence of direct slide agglutination from desoxycholate-citrate agar was variable, it was never used to obtain a preliminary diagnosis.

Discussion.

The appearance of signs and symptoms of relatively severe toxæmia in a comparatively large percentage of cases (47%) is unusual for dysentery in the South-West Pacific Area, unless one is dealing with infection by Shiga's bacillus. The occurrence of toxæmia raises the question whether or not Schmitz's bacillus produces an exotoxin.

Buchwald[6] has described the preparation of an exotoxin from old culture filtrates of *Shigella schmitzi* by precipitation with trichloracetic acid. The precipitate was redissolved in one-tenth of the original volume of saline solution, and on intraperitoneal injection of 0·01 millilitre of this solution into mice, death usually occurred within forty-eight hours. Paralysis of the hind legs frequently preceded death of the mice. The toxin was thermolabile, being destroyed by heating for one hour at 90° to 100° C.

Schröer,[7] in a more detailed and extensive study, obtained results similar to those of Buchwald, and both investigators concluded that, in order of toxicity, *Shigella schmitzi* should be placed half-way between *Shigella shigæ* on the one hand and *Shigella flexneri* on the other.

The toxæmia and neurological signs seen in our cases were probably caused by an exotoxin of the type described by Buchwald and Schröer. It is a matter for regret that the strains isolated from our patients are no longer available for testing for exotoxin production.

In view of the fact that *Shigella schmitzi*, *Shigella shigæ* and *Shigella Newcastle* are all mannite non-fermenting types, it would be interesting to know whether the last-mentioned also produces an exotoxin of the type described above.

Summary.

An outbreak of bacillary dysentery caused by *Shigella schmitzi* is described. In three months 51 patients were admitted to hospital.

Varying degrees of toxæmia were shown by 24 patients, and in 33 cases the sigmoidoscopic findings were normal. This is submitted as evidence that *Shigella schmitzi* produces an exotoxin, as suggested by other workers.

The laboratory procedures adopted are described in detail.

Acknowledgements.

We are deeply indebted to Colonel H. Hume Turnbull, consultant physician, Australian Military Forces, without whose encouragement and help in obtaining records this paper could not have been written. Our thanks are due to all members of the medical division of the Australian general hospital where this work was done, particularly to Captain W. F. Tomlinson, and to the Royal Australasian College of Surgeons for invaluable help in obtaining references. Major-General S. R. Burston, Director-General of Medical Services, has kindly given permission for the publication of this paper.

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THE COLOUR OF THE "GREY" MATTER OF THE BRAIN.

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THE colour of the cortex of the brain has never appeared to me to be grey. I should be more inclined to describe it as a light brown or greyish brown. It occurred to me, therefore, to try to match the colour of the cortex with the plates in Ridgway's "Color Standards and Color Nomenclature".[1] It is, of course, difficult to match the tints exactly. However, I found that a good way was to put a piece of brain into a test tube, when it could be readily compared with the plates. In twelve cases the colour was put down as follows: Vinaceous Fawn (Plate XI), five cases; near Vinaceous Fawn, three cases; Vinaceous Buff, one case; Light Vinaceous Fawn, one case; near Buff Pink (Plate XXVIII), one case; Pinkish Buff (Plate XXIX) or between Pale Ochraceous Salmon and Ligh Ochraceous Salmon (Plate XV), one case. The colour,

[1] The colours spelt with upper case letters are those used by Ridgway.

therefore, is not a grey colour but a Vinaceous Fawn. This colour misdescription led me to try to ascertain how the error arose.

Alexander Monro, junior, in 1813, in his "Outlines of the Anatomy of the Human Body",(1) described the cortex of the cut surface of the brain thus:

> The brain, when divided by an incision, is found to be neither uniform as to colour nor consistence. The outer part of it is somewhat of a colour resembling burnt wood; but internally white.

Robert Knox in 1828, in his translation of H. Cloquet's "A System of Human Anatomy",(2) in describing the substance of the brain, states that it presents two distinct modifications, one being a "soft, spongy and seemingly vascular substance, of a greyish colour, named the *Cineritious* or *Cortical Substance*, most commonly forming a kind of superficial envelope to the different parts of the organ, but also distributed through different parts of its interior". "Cineritious" really means the colour of ashes. "The Penny Cyclopædia", published in 1839, in describing the brain, states that "the outer substance is sometimes termed cineritious, it being of a greyish brown colour". "The Standard Oxford Dictionary" gives the following examples of the use of the term "grey" matter for the cortex:

1840. C. Ellis, *Anat.*:
45. The grey matter of the third ventricle entirely conceals the corners of the fornix.

1894. A Robertson, *Nuggets, etc.*:
33. These . . . thoughts rushed over the grey matter of Bill's brain as the wind rushes through the tree-tops.

1897. Mary Kingsley, *W. Africa*:
673. Whether he does this by adding convolutions or piling up his grey matter we will leave for the present.

Summary.

The colour of the cortex of the brain approaches the Vinaceous Fawn of Ridgway's "Color Standards and Color Nomenclature". "The Penny Cyclopædia's" "greyish-brown colour" is a good description, the tint being more a greyish brown than a brownish grey.

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(1) A. Monro, junior: "Outlines of the Anatomy of the Human Body", 1813, Volume III, page 126.
(2) R. Knox: "A System of Human Anatomy, Translated from the French of H. Cloquet", 1828, page 414, paragraph 1452.

OBSERVATIONS ON THE PART PLAYED BY THE VASOCONSTRICTOR SUBSTANCE OF BLOOD PLATELETS IN THE MECHANISM OF VASCULAR SPASM.[1]

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VASCULAR SPASM, which is of interest to the surgeon as an association of trauma or embolism, has been the subject of recent articles and reviews (Cohen, 1944) which indicate that its mechanism is still unknown. It would be an attractive hypothesis to consider that the contraction of the vascular walls in these conditions is attributable to a humoral agent liberated by tissue injury within the lumen, wall, or vicinity of vessels. In the search for such an agent one is led to examine the vasoconstrictor substance of defibrinated blood or serum. This substance, which depends for its formation on the presence of blood platelets (Janeway, Richardson and Park, 1918; Reid and Bick, 1942; Zucker, 1944), may be formed when blood is shed from a vessel, or when platelets break up in or on the walls of damaged or diseased vessels.

This paper is concerned with determining whether vascular spasm may be produced by this agent.

[1] Technical assistance was provided by a grant from the National Health and Medical Research Council.

Methods.

Cats and dogs were used. After preliminary ether anæsthesia the cats were anæsthetized with chloralose given intravenously, or were decapitated. Likewise, the dogs were given chloralose with or without a preliminary injection of ten milligrammes per kilogram of morphine. The animals were maintained under artificial respiration and the blood pressure in a carotid artery was recorded with a mercury manometer. The femoral artery was exposed in the femoral triangle and sometimes the anterior tibial artery in the leg. The rate of venous outflow from the hind limb was measured by the method of Feldberg and Schilf (1930). This consists of cannulating the femoral vein and returning the blood therefrom by tubing to a reservoir connected to the external jugular vein, the blood having been rendered incoagulable by means of an injection of heparin. The outflow into the reservoir is measured in drops or millilitres per minute. For intraarterial injections into the peripheral field of the femoral artery, the cut stump of the lateral circumflex artery was cannulated and injections were made through it into the femoral artery. Before the experiment was set up, blood was removed from the carotid artery for the preparation of serum or defibrinated blood to test on the same animal, in the manner described under the results.

Results.

The Effect of Serum or Defibrinated Blood Placed Around an Artery.

In no case (eight cats and four dogs) did serum or defibrinated blood when placed around the femoral or anterior tibial artery, over lengths up to four centimetres, reduce the outflow from the hind limb. Likewise no visible effect on the diameter of the vessel was observed, although earlier the same artery had sometimes exhibited a transitory spasm for a few minutes during the setting up of the experiment. In one experiment (dog) the blood pressure was recorded in the anterior tibial artery while serum was placed around the femoral artery. No change occurred in the mean blood pressure in the former vessel.

Effect of Serum Injected Intraarterially.

When serum in quantities of 0·5 to 2·0 millilitres was injected intraarterially into the cut stump of the lateral circumflex artery of nine cats and three dogs, including those which had shown no response to serum applied to the femoral artery, there resulted a sharp fall in the outflow from the hind limb, which in the absence of a commensurable fall in systemic blood pressure or change in capacity can be attributable only to vasoconstriction. Figure I shows the systemic arterial blood pressure in a cat weighing 3·4 kilograms. At the hatched area the cat's serum was placed around the main vessels in the right femoral triangle over a length of approximately three centimetres. At the first arrow one millilitre of normal saline solution and at the second arrow one millilitre of cat serum were injected intraarterially. Usually, as in this case, the vasoconstriction was preceded by transient vasodilatation.

Influence of Other Factors.

Anæsthesia.—It was thought possible that more definite results may have been obtained had the animal not been anæsthetized. To exclude the influence of the anæsthesia, two more cats were anæsthetized with ether and decapitated, and after recovery from the ether, serum was injected intraarterially or placed around the artery both before and after the intravenous injection of chloralose. This anæsthetic agent had no effect on the responses to serum.

Occlusion of the Main Artery.—Again, it was thought that more marked effects might be produced if the circulation to the limb was occluded during and for some time after the intraarterial injection. Occlusion of the common femoral or iliac artery by means of a clip, for periods up to ten minutes after the injection of up to five millilitres of serum, had no effect in increasing or prolonging the vasoconstriction which was demonstrable after the circulation had been released, but usually the preliminary vasodilatation did not occur. Likewise occlusion of the main

vessel did not affect the action of serum placed around the main vessel distal to the occlusion.

Heparin.—It was found that the placing of serum or defibrinated blood around the femoral artery produced no change in the diameter of the vessel whether the animal was given heparin or not. It was also shown that when an artery was divided in an animal which had received heparin, contraction of the vessel wall and hæmostasis occurred while the arterial blood pressure remained high. Subsequent redivision of the vessel resulted in further bleeding. Thus in one experiment, a muscular branch of the femoral artery was divided, the blood being mopped up with successive packs of cotton wool. Hæmorrhage ceased after 4·5 minutes, the arterial blood pressure having fallen from 128 to 88 millimetres of mercury in the interval and risen to 104 millimetres of mercury when hæmorrhage ceased. Division of the vessel higher up and of the corresponding vessel in the opposite limb caused fresh hæmorrhage from each site.

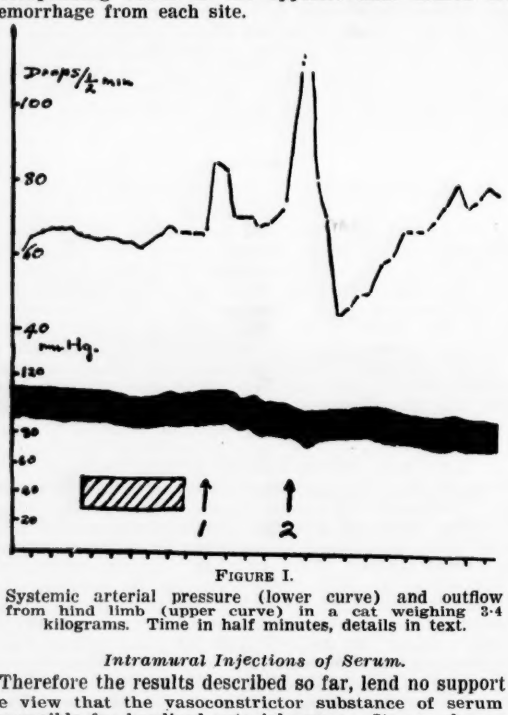

FIGURE I.

Systemic arterial pressure (lower curve) and outflow from hind limb (upper curve) in a cat weighing 3·4 kilograms. Time in half minutes, details in text.

Intramural Injections of Serum.

Therefore the results described so far, lend no support to the view that the vasoconstrictor substance of serum is responsible for localized arterial spasm. It may, however, be argued that in some at least of the conditions under which spasm occurs, the active substance may be liberated in much more intimate relationship with the muscle of the vascular wall than has been possible in these experiments. Therefore, serum or defibrinated blood was injected with a fine hypodermic needle into the wall of the femoral artery; it did not cause contraction.

Mechanical Stimulation of the Artery.

It has already been stated that sometimes mechanical stimulation of the vessel by forceps during the setting up of the experiment resulted in a transitory spasm. As attempts to cause local spasm by local application or intramural injections of serum had failed, it was necessary to determine whether an artery which had failed to respond to these stimuli could be made to contract by other means. Mercury drops were allowed to fall onto the artery from a burette, the tip of which was ten centimetres above it, a total mass of 300 to 600 grammes falling in the space of two to five minutes. This form of stimulation was effective in one out of three cats. In two out of four experiments (including the one in which mercury stimulation was effective), beating of the femoral artery with a small mallet caused local spasm. The mercury drops were allowed to stimulate the artery alone, which had been placed in a paraffin gutter. This was not possible with the mallet experiments, so that the spasm which resulted in these two experiments may have been reflex in origin from stimulation of the surrounding tissues. Nevertheless, in one of these two experiments the femoral and sciatic nerves were divided during the duration of the spasm without its being affected. In this experiment the spasm and the diminished outflow persisted for ten minutes before division of the nerves, and for twenty-one minutes thereafter. In neither of these animals (two cats) were the spasm and diminished outflow associated with macroscopic damage to the vessel wall.

Figure II shows the blood pressure in a carotid artery and the outflow from the femoral vein of a cat. At *A*, 2·0 millilitres of serum were injected intraarterially; between *B* and *C* the femoral artery was stimulated by mercury drops, and at *D* by being beaten with a mallet. After the last-mentioned procedure the artery was reduced to a narrow thread and the outflow to zero; this condition persisted till the termination of the experiment, fifteen minutes later.

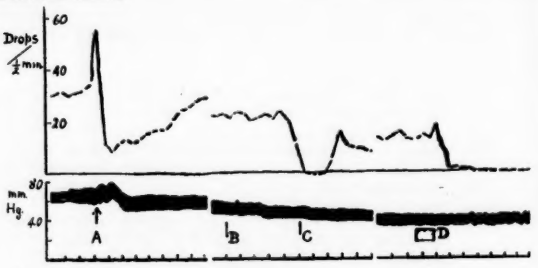

FIGURE II.

Systemic arterial blood pressure and outflow from the hind limb in a cat weighing 2·5 kilograms. Time in half minutes, details in text.

Discussion.

Vascular spasm may be associated with a number of local conditions in the artery, including those due to trauma, thrombosis or embolism. In general, it may be stated that the spasm may be attributable to either of two causes: (i) stimulation of nerve fibres in the wall of the vessel, resulting in constriction either directly or by reflex means; (ii) stimulation of smooth muscle by an adequate mechanical stimulus or by a humoral agent. In either case the vascular constriction which results may be localized to a segment of artery or may involve its peripheral field or collaterals.

This paper is not mainly concerned with the investigation of possible reflexes from mechanically stimulated arteries. A review of the evidence by Cohen (1944) indicates that a reflex basis for many of the cases of vascular spasm does not exist. Cohen points out, for example, that the vessels are not regularly released by local or spinal anæsthesia, and even when relaxation is reported to take place, it is often delayed for several hours. Moreover, he emphasizes that spasm characteristically persists for long periods, even in the amputated limb, where one would expect the nerve fibres to cease conduction. Some of Cohen's arguments will also apply to direct stimulation of smooth muscle in the vessel wall, for unless the stimulus is continuous it is not easy to explain why spasm should persist for such long periods. However, it should be pointed out that the persistence of spasm for long periods is not necessarily an argument against a transient stimulus of either muscle or nerve. It may, for instance, be characteristic of some vascular walls that once contracted they relax slowly, the rate of relaxation depending on the magnitude of the distending pressure. That this may be so is indicated by the results of many of my observations on the isolated carotid artery of the ox. When these vessels are removed shortly after death and placed in Ringer's solution, some merely "collapse", while others become firmly contracted and remain so for days. In either case arterial rings cut from the vessel and suspended in

Ringer's solution may be used as test objects after preliminary stretching (Meyer, 1906; Reid and Bick, 1942). When rings from the former kind of vessels are used, usually they relax in some ten to twenty minutes after stimulation by adrenaline or serum, whereas ring preparations from the latter type of vessel frequently do not relax for several hours after stimulation, or the relaxation may be interrupted by further contraction. In general, also, relaxation becomes progressively slower with either type of vessel the longer the preparation remains set up.

In view of the slow relaxation of some vessels, it would appear that a transient reflex or direct stimulation cannot be ruled out as the initiating factor. Cohen himself does, in fact, place in a different category the vascular spasm met with in crush injury or following the application of tight tourniquets, as in the experiments of Barnes and Trueta (1944). In such cases the vessels may not appear damaged, and the suggestion is made that the vascular constriction is reflex in origin from damaged skin and deeper tissues. In the experiments of Barnes and Trueta, the constriction did, in fact, involve the hind limb of the rabbit opposite to the one on which a tight wire tourniquet had been applied.

Nevertheless, in some conditions at least an adequate mechanical stimulus has not been defined, as, for example, in the vascular constriction which takes place distal to an embolus (Linton, 1941). As Lewis (1936) points out, the impact of a relatively soft embolus is not likely to provide the stimulus. It is possible that the sudden fall of pressure beyond the occlusion may be responsible, but there is no evidence for this; in fact, the common procedure of occlusion of a vessel by a spring clip does not cause spasm distal to the clip.

The main question for discussion here is whether spasm, either locally or in the peripheral field of the damaged vessel, may be attributable to a humoral agent derived from blood platelets and present in shed blood. So far as local spasm is concerned, it has not been possible to affect either the artery or the blood flow from the limb by placing serum around a main artery, or by intramural injection, whereas on the other hand it has been possible in the same animal, without bruising of the vessel, irregularly to cause local spasm with diminished blood flow by various form of mechanical stimulation. These results would indicate that this particular humoral hypothesis is untenable.

The peripheral field of the damaged artery must also be considered. Thus it is possible that when platelets break up on damaged endothelium, or when small thrombi form, active substances causing vasoconstriction are carried into the distribution of the injured vessel. It is well known that perfusion of isolated limbs with defibrinated blood causes prolonged vasoconstriction, and in these experiments the intraarterial injection in the intact animal of small amounts of serum caused marked but transient vasoconstriction.

Therefore these experiments indicate that the humoral agent in shed blood is not responsible for localized arterial spasm. It may be a factor, if not the sole factor, in maintaining constriction in the peripheral field of an artery, damaged, thrombosed or occluded by emboli, provided that the circulation is inadequate to remove it or that it continues to be liberated. A further possibility is that the effects of spasm in a damaged artery or simple mechanical obstruction of it may be aggravated by a peripheral constriction interfering with a collateral circulation.

Recently Zucker has investigated the relationship of the vasoconstrictor substance in platelets to hæmostasis in arteries up to 210μ in diameter in the mesentery of the rat. She found that constriction of an incised vessel took place whether the animal's blood had or had not been made thrombocytopenic, and concluded that constriction of the vessels took place mainly as a result of the mechanical stimulus of cutting. On the other hand, she found that topical application of serum or platelet extract caused contraction of these vessels, and that a vessel lying beside the injured one also became constricted provided a platelet plug was formed. These results are not in disagreement with those reported in this paper, for I have been concerned with large vessels, so far as direct application of serum is concerned. That smaller vessels in the limb of an intact animal do become constricted in response to serum is shown by the results of intraarterial injection.

A further question for discussion relates to the part which spasm may play in some of the vascular accidents familiar to the physician. Trethewie (1947) has recently shown that heparinized blood perfused through the heart or brain does not acquire anticoagulant properties conferred by other organs such as the liver or kidney. One is tempted to postulate that in the heart and brain a factor concerned in the production of occlusion of the small vessels is not necessarily thrombosis as such, but constriction produced by the vasoconstrictor agent liberated in the incipient stages of the clotting process, which is more prone to occur in these organs. This might, for example, explain the transient nature of some cerebral vascular accidents.

Summary.

Although serum or defibrinated blood causes contraction of isolated arterial strips, it is without effect when applied directly or injected intramurally into the femoral or anterior tibial artery *in situ*, in the cat or dog. This absence of effect in the intact animal is not due to heparin or to the anæsthetic agent used.

Some arteries which had failed to go into spasm on the application of serum did so on mechanical stimulation.

This result indicates that segmental arterial spasm is not due to a humoral agent in shed blood.

The intraarterial injection of serum in the intact animal causes constriction in the peripheral field. The significance of this observation in relation to vascular accidents is discussed.

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Reports of Cases.

BILATERAL VAGOTOMY: A PRELIMINARY REPORT IN A CASE OF DUODENAL ULCER.

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For many years peptic ulcers intractable to medical therapy have presented an unsolved problem. Until recently the variety of surgical procedures employed to relieve such lesions have not provided impressive results.

Patients with peptic ulcer have been observed frequently to have exacerbations of their symptoms at times of mental stress. This observation has led to the belief that there is a close correlation between the functions of

both cerebral cortex and stomach. It was Pavlov who showed that in dogs, after bilateral vagus section, gastric secretion in response to sham feeding and conditioned reflexes was lost. This suggests that the vagi form one of the main pathways, if not the most important, between the cerebrum and the upper part of the gastro-intestinal tract. Dragstedt later demonstrated that ulcer patients had an excessive and continuous secretion of gastric juice. Hypersecretion occurred at night and during resting hours, when the gastric secretion, frequently more acid than normal, was not neutralized by food. Although he suggests that the cause of this hypersecretion may be related to a continuous absorption of chemical gastric secretory stimuli such as histamine, in view of Pavlov's experiments it is more likely that the vagal stimuli are responsible. Work on both animals and humans has formed the basis on which Dragstedt[1][2][3] and his co-workers developed the technique of transthoracic supradiaphragmatic transsection of the vagus nerves. This operation, although still in the experimental stage, appears to have given persistent relief of ulcer distress; but the passage of time alone will show its success in avoiding the return of the ulcerating tendency.

Clinical Record.

Early Clinical History.

The patient was a well-nourished, well-developed, apparently healthy bank officer, aged thirty-nine years. During 1938 he noticed a gradually increasing gnawing sensation low in the epigastrium and to the right of the umbilicus, which he described as "hunger pains" recurring half to one hour before meals. For the last six years the pain had recurred progressively closer to the previous meal, and at the time of his admission to hospital in February, 1946, it occurred one hour after meals. The pain was relieved usually by food or alkalis. Recently episodes of two or three weeks' duration had occurred every two or three months, during which the pain had been more severe than previously and unrelieved by food or alkalis. Two years earlier he had a hæmatemesis to the extent of about five ounces. This had not been repeated. There was no history of tarry stools; on the contrary, usually the stools had been pale.

Radiological examination confirmed the presence of a duodenal ulcer, which, in spite of two periods of thorough medical therapy (including one previous stay in hospital) and a rigid dietetic *régime*, remained unhealed.

The ulcer undoubtedly appeared to be of the type associated with overactivity and hyperacidity of the stomach. The history is interesting in this respect.

In conversation with the patient it is evident that his alimentary tract has been excessively influenced by his mental state since boyhood, any excitement causing "bilious attacks". In later life the same state existed; he was unable to sleep on the night prior to a golf match, and during matches he frequently had such severe abdominal discomfort and pain that he was unable to continue playing; consequently, the patient now forgoes the pleasure (or otherwise) of golfing. It may be more than coincidental that two years prior to the onset of his symptoms the patient married, and he soon realized that he and his wife were temperamentally incompatible, frequently disagreeing bitterly; during these episodes the pain was most severe. In 1938 it became obvious that his wife was sterile owing to occlusion of the Fallopian tubes. It is not hard to believe that the mental strain associated with business and social activities coupled with domestic incompatibility and finally thwarted parentage culminated in the development and persistence of the patient's ulcer.

Recent Clinical History.

After his admission to hospital the patient was given a "soft" ulcer diet, alkalis and belladonna. Symptoms were relieved slightly, but the epigastric pain recurred regularly prior to the two-hourly feedings. His psychological outlook did not improve, and the patient became even more introspective than previously and took morbid interest in describing his dyspeptic symptoms in detail.

X-ray examination revealed a small filling defect at the base of the duodenal cap suggesting an ulcer crater. A fractional test meal examination (Figure 1) showed that both total acid and free acid were much increased above normal limits. Tests for occult blood gave positive results during the first week after his admission to hospital, but later the results became negative.

As the ulcer appeared to be of the vagotonic, unresponsive type, unassociated with pyloric obstruction, it was considered ideally suited to treatment by bilateral vagotomy.

Surgical Procedure.

The thorax was opened on the left side after the resection of the eighth rib under cyclopropane and ether endotracheal anæsthesia. The left lung was relaxed and retracted superiorly while the œsophagus was identified between the left ventricle of the heart and the aorta. The lower end of the œsophagus was found to be much dilated and thought to be a thoracic stomach. The pleura was incised over the œsophagus for approximately two inches and the œsophagus was mobilized. The left vagus nerve was identified on the antero-lateral aspect of the

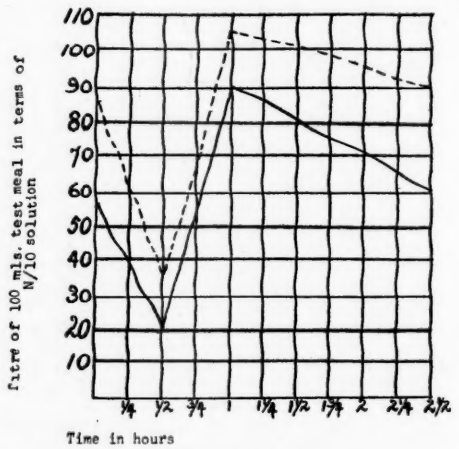

FIGURE I.

Continuous line, free acid; interrupted line, total acid.
Resting juice, 120 millilitres, blood present.

œsophagus, dissected free, injected with "Planocain", ligated and cut. The proximal and distal ends were tucked up and down respectively under the pleura. The right vagus was isolated from the postero-medial aspect of the œsophagus and treated likewise. The pleura overlying the œsophagus was closed with interrupted cotton sutures. Penicillin (30,000 units) was injected intrapleurally as a precautionary measure and the cavity was closed in layers by the usual method.

At the conclusion of the operation, thin, brownish, regurgitated fluid similar to altered blood was found in the patient's mouth and nose, and when a bronchoscope was passed similar material was sucked from both mainstem bronchi.

The patient's condition during the operation was fair, no appreciable difference occurring in pulse rate or blood pressure after severing of the vagi.

Post-Operative Period.

After operation the patient had dramatic relief of his ulcer pain. For the first few days he continued to receive frequent small feedings as previously, but later he was allowed an unrestricted diet, and still there was no return of epigastric discomfort. The only complications were intercostal pain and slight surgical emphysema. The pain occurred along the seventh and eighth left thoracic segments and was rather severe and persisted for the first week, but was relieved by pethidine and opium. Emphysema around the wound was also seen radiologically in the mediastinum, but this subsided in a few days.

X-ray films taken after a barium meal on the twelfth day after operation showed a persistent deformity consistent with cicatrization at the base of the duodenal cap. The stomach motility was less than normally found. The emptying time was six hours. Unfortunately there are no pre-operative records of motility or emptying time which could be used for comparison.

A functional test meal examination was performed ten days after operation, and it is interesting to note the pronounced reduction in the amount of both free and total acid (Figure II). There was also a considerable increase after operation in the amount of resting juice, from 120 to 210 millilitres.

The patient was discharged from hospital on the fifteenth day after operation, feeling well and free from all pain. He was interviewed one month later, and in spite of taking irregular meals with intervals as long as five hours,

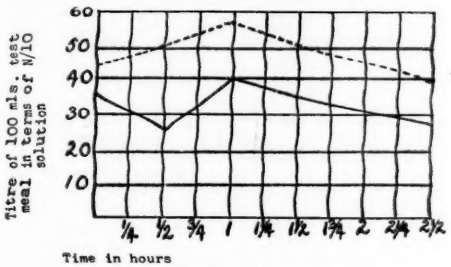

FIGURE II.

Continuous line, free acid; interrupted line, total acid. Resting juice, 210 millilitres, blood present.

an unrestricted diet and no alkaline powders, and in spite of heavy mental strain, he had had no return of epigastric discomfort or pain. The patient is now able to lead a normal life, and to carry on his business, social and domestic affairs with uninterrupted success.

Discussion.

Owing to limited knowledge about the later sequelæ of bilateral vagotomy, it is impossible to state its full limitations. However, at present it appears to be contra-indicated in the presence of acute perforation, acute severe hæmorrhage and cicatricial obstruction. It is also thought that gastric ulceration proximal to the pylorus should be treated with caution, as it is frequently difficult if not impossible to distinguish ulcer from carcinoma.

According to workers at the Massachusetts General Hospital,[3] previous ulcer surgery does not complicate the operation; on the contrary, patients who have previously undergone pyloroplasty, posterior gastro-jejunostomy and gastric resection with return of the ulceration, are ideal subjects for vagus section. Young or middle-aged men with a long history of ulcer unassociated with obstruction, who have been resistant to medical therapy and who have exacerbation of symptoms at times of mental stress, appear to obtain a good result from this procedure.

Summary.

The rationale of supradiaphragmatic resection of the vagus nerve for peptic ulcer is briefly mentioned. In one case such an operation proved successful after a short follow-up period. The clinical history and surgical procedure relating to this case are fully discussed.

It is hoped that supradiaphragmatic vagotomy will be of value in preventing the return of peptic ulceration. It is hoped also that the presentation of this case will stimulate closer cooperation between physicians and surgeons in selecting patients suitable for operation, thus providing the data so necessary for estimating the full worth of this procedure.

Acknowledgements.

My thanks are due to Dr. B. T. Shallard, the physician attending the patient, and Dr. M. P. Susman, the surgeon who performed the operation, for their help and suggestions. Also I wish to thank Dr. J. R. Radcliffe, Medical Superintendent of the Royal North Shore Hospital of Sydney, for permitting this report to be published.

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(1) L. R. Dragstedt and P. W. Schafer: "Removal of Vagus Innervation of Stomach in Gastroduodenal Ulcer", *Surgery, Volume XVII, 1945, page 742.*

(2) L. R. Dragstedt: "Vagotomy for Gastroduodenal Ulcer", *Annals of Surgery*, Volume CXXII, 1945, page 973.

(3) F. D. Moore, W. P. Chapman, M. D. Schultz and C. M. Jones: "Transdiaphragmatic Resection of Vagus Nerves for Peptic Ulcer", *The New England Journal of Medicine*, Volume CCXXXIV, 1946, page 241.

Reviews.

A TEXTBOOK OF MEDICINE.

CONYBEARE'S "Textbook of Medicine" is an outstanding example of what an extraordinary amount of current medical knowledge can be packed into a comparatively small volume, if a painstaking selection of the essential information about each subject treated is made.[1] For this, no doubt, Sir John Conybeare, the editor, has largely to thank his contributors, but he in turn is to be congratulated upon his wisdom in selecting his team.

The fact that we are reviewing the eighth edition only eighteen months after the seventh was issued is very clear evidence that this is such a widely used textbook that it needs to be kept right up to date. A very welcome addition to the new volume is an appendix on aviation medicine by Wing Commander R. H. Winfield, which is excellently written and should be of great value to practitioners as well as to students.

In the review of the previous edition regret was expressed that it had been decided to omit an extended reference to penicillin, but no fault can be found on that score with the book now being discussed. Sir John Conybeare has himself written a special section dealing with this new form of chemotherapy, while its therapeutic value, with full details of its employment in pneumonia, septicæmia and subacute bacterial endocarditis, is adequately dealt with in the chapters dealing with these diseases.

The sections dealing with disorders of the endocrine glands have been revised and a remarkable amount of information is supplied in the limited space available.

A valuable minor addition to the new edition is found on the inside of the front cover in the form of a table of physiological normal findings in blood chemistry, in blood, cerebro-spinal fluid, urine and fæces, where they will surely be useful for reference purposes.

We have no hesitation in describing this as outstanding among shorter textbooks of medicine and in recommending it to both students and general practitioners.

PHARMACOLOGY, MATERIA MEDICA AND THERAPEUTICS.

THE seventeenth edition of "R. Ghosh's Materia Medica and Therapeutics" follows the general line of previous editions, but has been subjected to extensive revision and includes details of several new subjects.[2]

In its 800 pages is a fund of well classified and indexed information—pharmacological, therapeutic and pharmaceutical—rarely to be found collated in one volume. The selection of material forming the bulk of the book is excellent, despite the retention of a number of discredited medicinal agents, included probably to complete the reference value of the work.

A section on Indian indigenous drugs—many of them at one time official in the British Pharmacopœia and its Indian addendum—gives the only indication as to the geographic origin of the volume.

[1] "Textbook of Medicine", by Various Authors, edited by Sir John Conybeare, K.B.E., M.C., D.M. (Oxon.), F.R.C.P.; Eighth Edition; 1946. Edinburgh: E. and S. Livingstone, Limited. 8¼" × 5¼", pp. 1178. Price: 30s.

[2] "Pharmacology Materia Medica and Therapeutics (R. Ghosh's Materia Medica and Therapeutics)", by Birendra Nath Ghosh, M.B.E., F.R.F.P. and S. (Glasgow), F.R.S. (Edinburgh); Seventeenth Edition; 1946. Calcutta: Hilton and Company; Sydney: Angus and Robertson, Limited. 8½" × 5¼", pp. 830, with illustrations. Price: 21s.

In Part I, "Materia Medica Proper", are comprehensive tables summarizing most of the essential pharmacopœial details requisite for reasonable prescribing, while, with the appropriate monographs in the therapeutic section, are featured lists of incompatibles, practical prescribing hints, with illustrative prescriptions and many unofficial preparations and formulæ culled from the British Pharmaceutical Codex and other sources.

The main body of the book dealing with pharmacological data and their therapeutic interpretation is direct and concise and adequately covers the subject. Students will appreciate the many tabulated summaries comparing and contrasting the actions of related drugs.

Items of interest among the newer compounds are the sterols, dehydrocholic acid as a cholagogue, sodium dehydrocholate to estimate circulation time, and dihydrotachysterol with prothrombin-like action; protein hydrolysate as a source of protein in starvation; dicumarin as an anticoagulant; thiouracil and its derivatives in thyreotoxicosis; and a diverse group of parasiticides including DDT, lauryl thiocyanate, lethane and derris.

Penicillin naturally receives much attention, and the monograph includes practical pharmaceutical and administrative details. There is little reference to the increasing number of side reactions now accumulating in reports. Streptomycin and related antibiotics have not as yet found a place in this comprehensive work.

Dr. B. N. Ghosh, whose association with this work dates from its sixth edition in 1915, is to be congratulated on his production of a treatise having such a wide sphere of practical utility.

PARENTERAL ALIMENTATION IN SURGERY.

ROBERT ELMAN'S book on "Parenteral Alimentation in Surgery" contains a thorough digestion and metabolism of the voluminous literature on the subject and is an integrated presentation of present-day knowledge.[1]

While it is now well known that protein deficiency and hypoproteinæmia are deleterious to the patient who has been operated upon, Professor Elman gives detailed consideration to many other factors necessary to ensure the smoothest possible post-operative convalescence.

Vitamin *C* is most important in wound healing, and disappears from the plasma of the normal patient within three days of a severe operation. This rapid utilization of the vitamin following operation or injury does not seem to be generally recognized. He also brings some evidence to show that circulatory impairment follows a low level of vitamin *C*. The average daily requirement of vitamin *C* is 50 to 160 milligrammes, but in malnourished patients up to 1·0 gramme a day is necessary for several days after operation, followed then by 100 milligrammes twice a day. In cases of severe burns as much as 2·0 grammes a day has been found to be necessary. There would appear to be no deleterious effects from overdosage.

Vitamin B_1 (thiamin) is particularly needed by patients who are having intravenous injections of glucose, as it has been shown that intravenous alimentation with glucose produces a marked depletion of all *B* vitamins. The result of marked vitamin *B* deficiency is vomiting, diarrhœa, anorexia *et cetera*. The usual daily dose is 1·5 milligrammes, but when deficiency is present (as after an operation) as much as ten milligrammes a day should be given for a few days. Again there would appear to be no deleterious effects from overdosage.

One to two milligrammes of riboflavin are required each day, and 25 milligrammes a day of niacin, rising after an operation to 50 milligrammes a day for several days.

The author mentions that severe hepatic insufficiency precludes the production of prothrombin in the liver regardless of the amount of vitamin *K* injected. (This is the basis of the vitamin *K* hepatic function test.) Thus, in severe liver damage, large doses of vitamin *K* will not inhibit the tendency to bleeding.

The only vitamins that Elman considers of surgical importance at present are vitamin *C*, vitamin B_1, vitamin B_2, niacin and vitamin *K*.

He has much to say about the parenteral administration of amino acids. The first acid hydrolysates were used in 1937, but the acid destroyed some of the amino acids, and now an enzymatic hydrolysate of casein is available.

The indispensable amino acids in protein are lysine, tryptophan, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, valine and arginine. Amino acid mixtures, just as any other protein given by mouth, are not properly deaminized in the presence of profound liver disease and are excreted. Mixtures of the commercially available chemically pure amino acids are far too expensive at the present time. Elman mentions the use of "Amigen", a commercial hydrolysate containing amino acid and peptides. He records only 22 untoward reactions with this solution among 362 patients.

The main contraindication to injections of amino acids is the presence of turbidity or precipitation; only crystal-clear solutions should be injected. Occasionally amino acids may be employed to augment the oral intake of proteins. Elman states that patients who had had careful alimentation and parenteral amino acid administration lost negligible weight after operation and did not require prolonged convalescence.

On the presentation side, this important book follows the excellent modern practice of combining clear type with unequivocal and simple "visual aids" and line diagrams, and a chapter-by-chapter bibliographical documentation of the facts presented.

[1] "Parenteral Alimentation in Surgery: With Special Reference to Proteins and Amino Acids", by Robert Elman, M.D.; 1947. New York, London: Paul B. Hoeber, Incorporated. 9¼" × 6", pp. 306. Price: $4.50.

RADICAL SURGERY IN ABDOMINAL CANCER.

THE Hippocratic aphorism, "For extreme diseases, extreme methods of cure are most suitable", has been acted on to a noteworthy degree by Alexander Brunschwig, of Chicago, and the story is told in his book on "Radical Surgery in Advanced Abdominal Cancer".[1] The book is a record of achievement that should attract the attention of all surgeons, as it shows the unexpected lengths to which one may at times go successfully. Particularly should it be read by all young surgeons, for it should be a source of inspiration to them as was Grey Turner's little book "Encouragements in Cancer Surgery" to their fellows of an earlier generation. Attention is called to the fact that the discovery of "inoperable" disease does not end the surgeon's responsibility to any patient, as frequently there is much he can do to palliate the disease and so lessen the patient's suffering. He may even succeed in prolonging life to an unexpected degree.

Previously, much of this surgery was impossible, but with present-day knowledge of the deficiencies and how they can be treated, with adequate methods of treating shock, and with anæsthetic methods that can provide relaxation for several hours, operations that include removal of much of several organs are possible and may give a good result, provided certain vital structures are left intact. The pancreas no longer has *noli me tangere* written along its length—it may safely be resected either in whole or in part, either for intrinsic disease or for a disease invading it from adjacent organs. Direct spread to the liver may no longer constitute an impassable barrier to the resection of advanced tumours of the stomach, gall-bladder and colon. The stomach, nevertheless, still provides the surgeon with a relentless opponent, and extensive resections of this organ are not nearly so likely to be successful as are resections for advanced carcinomata of the colon, which will frequently give good results after very unpromising starts.

Brunschwig details the history, pathological findings and operative details of one hundred consecutive cases of advanced carcinoma of the abdominal organs, usually involving more than one viscus. Of the patients, nineteen are living for periods varying from two to ten years, thirty received some degree of palliation, the condition of twenty was not improved, and thirty died as the direct result of the operation. The operative mortality may be thought heavy, but is counterbalanced by a consideration of what was being attempted, and by a realization that most of these patients had but a short period of painful existence before them. What is important is the degree of success achieved—20% of apparent cures and 30% of palliations among patients that would ordinarily be classified as inoperable.

The idea behind the book is important, as we still have no cure for abdominal cancer but the knife. With the increasing average age of the population cancer is becoming a very common disease, and this means that more and more of the population will require surgical aid for it. Thus it is very important that more and more of our surgeons should acquire what Gordon Gordon-Taylor calls the cancer outlook possessed to such a remarkable degree by the author of this book.

This is a book that should be read at least once by every abdominal surgeon.

[1] "Radical Surgery in Advanced Abdominal Cancer", by Alexander Brunschwig, M.D.; 1947. Chicago, Illinois: The University of Chicago Press. 9½" × 6½", pp. 336, with many illustrations. Price: $7.50.

The Medical Journal of Australia

SATURDAY, AUGUST 2, 1947.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE PROPOSAL TO ESTABLISH A MEDICAL SCHOOL IN WESTERN AUSTRALIA.

In the issue of January 18 of this year the proposal to establish a medical school in Western Australia was discussed in these columns. It was pointed out that the Government of the State was aware of the need for a medical school within its borders, and statements of the Premier, showing his understanding of the problem, were quoted. It will be remembered that in July, 1946, the Premier of Western Australia invited Professor Peter MacCallum, Professor of Pathology and Dean of the Faculty of Medicine in the University of Melbourne, to make a personal investigation and to advise the Government. Professor MacCallum's report was submitted to the Premier in October, 1946, and subsequently printed. He recommended the establishment of a medical school as highly desirable and practical, provided the proposed school was of university standard throughout and conformed to university ideals. Our discussion in January was based chiefly on Professor MacCallum's report. Those who are interested in the subject are referred not only to our editorial, but also to Professor MacCallum's president's address to the Victorian Branch of the British Medical Association, published in the same issue. This address dealt with "The University and Clinical Teaching" and Professor MacCallum insisted that no system of clinical teaching could succeed if inspiration was lacking. In the opinion of many who ought to know, inspiration will not be lacking in Western Australia when, to quote the editorial in this journal, a school "founded in faith and hope with firmness of will and complete understanding" comes into being.

Hopes having been raised by the sincerity of the Western Australian Government and by the encouraging report of Professor MacCallum, keen disappointment has been felt at the announcement by the Government that it has had to postpone the establishment of a medical school. *The West Australian* has stated that the main reason given by the Premier for the postponement is the priority of the claims for housing, the contention being that the first call on building labour and materials should be for new homes "to relieve the acute shortage which is causing severe inconvenience, waste of money or actual hardship for so many people in city and country". If a choice had to be made by all persons in the community between the provision of homes for the people and the erection of a medical school, it is safe to say that practically everyone would favour the former. The medical profession throughout the Commonwealth has declared that housing is one of the fundamental needs that has to be met before medical attention as such, in the preventive and curative spheres, can hope to be effective. Since many people of the present day think and speak of the satisfying of human needs in terms of "priority", a word around which tales of use and abuse may be told, we may say that, apart from the provision of food, housing should enjoy first priority. But if we grant that the Government of Western Australia is justified in its decision, we must not be content to sit back, to fold our hands in complacency and to worry no further. We know that the Government of Western Australia is alive to the need for a medical school, and it is reasonable to assume that it will do what it can to meet the need, provided that in so doing it does not interfere with the completion of its housing programme. To say that housing is to receive first priority does not mean that housing is to occupy the Government's attention to the exclusion of every other public duty. We may also assume that the building of a medical school stands high in the priority list. The Government will not readily forget Professor MacCallum's insistence that the foundation of a medical school was not only desirable, but was the most potent influence that could be introduced for the promotion of the health and social well-being of the people of Western Australia. In July, 1946, the Premier was at great pains to explain that students who intended to study medicine and were in fact engaged in the study of the first year of the course at the University of Western Australia, would have great difficulty in finding accommodation at the Universities of Melbourne or Adelaide to continue their studies. Last year, we understand, fifteen students who had completed their first year were unable to go on with the course. Their plight may have been due as much to overcrowding in the medical schools of the eastern States as to the financial burden which migration would impose. The Western Australian Premier expressed the opinion that the cost of study in this divided kind of way would prevent otherwise suitable students from undertaking the course.

Since the building of a permanent medical school has to be abandoned for the present, the question to be decided is what can be done in the meantime. In our discussion last January we indicated that great care would need to be taken if any temporary arrangements were contemplated. In regard to temporary buildings, a distinction must be drawn between buildings that are intended for four or five years' use and no more, and those somewhat more elaborate "temporary" affairs which are used for so long that they become in actual fact permanent. Buildings of the latter type are more costly in money and material than those of the former and cannot be considered at present for a Perth medical school. The really temporary buildings would be acceptable, provided the right kind of

teachers were appointed; it is the calibre of the teachers and the kind of teaching which really matter. Teachers in the new school should be men of undoubted ability from the academic and practical points of view. Though it might be possible to make plans in such a way that the erection of what we call really temporary buildings and the securing of equipment would be spread over three or four years as students who had started the course advanced in it, this would not be possible with all subjects. For example, a pathology department, with its specimens, macroscopic and microscopic, could not be built up overnight. A professor who was required to teach students in, let us say, three years' time, would need to be appointed almost at once, so that he would be ready for students to the stage of the course dealing with pathology. As a matter of fact, from the time of his appointment, a professor in pathology, by reason of his stimulating influence on practitioners in every branch of medical practice, would at once help to promote "the health and social well-being of the people of Western Australia". The Government of Western Australia has difficult decisions to make in this matter, but the difficulties are not insuperable, and the Government can rely on the cooperation of the medical profession.

Current Comment.

MOTION SICKNESS.

MOTION SICKNESS has always been a distressing problem and the suggested remedies are legion—a fair indication of the limited value of any one remedy. During the recent war the problem became a vital one to invasion forces and so received intensive study. R. L. Noble, E. A. Sellars and C. H. Best have now presented a report covering work sponsored by the National Research Council of Canada.[1] Extensive experimental work was carried out on large numbers of subjects. A long series of drugs was investigated, the majority being belladonna alkaloids or barbiturates; placebos were used extensively for control purposes. Their effects were observed on subjects both in specially constructed swings and at sea. The discussion is long and detailed, but reference will be made here only to the main practical conclusions. The effectiveness of hyoscine, which has been long recognized, is confirmed, but the investigators found reason to believe that a mixture of hyoscine and hyoscyamine might be given with less danger of unpleasant or dangerous side-effects than an equivalent dose of hyoscine alone. Individual tolerance varied, but in the case of healthy young men (11 stone) an initial dose of 0·3 milligramme of hyoscine hydrobromide *plus* 0·8 milligramme of hyoscyamine hydrobromide was effective, and apart from causing a dry mouth produced no adverse effects. The protection lasts for six to eight hours. It is considered that subsequent doses should not be more than one-half the initial dose, and should be separated by an interval of eight hours or more. The presence of a dry mouth is not regarded as a contraindication to further treatment. The usefulness of the barbiturates has long been accepted, but the drug which showed most promise in this group was ethyl β-methyl allyl thiobarbituric acid, known as V-12, which had the additional virtue of possessing a low depressant action. There is considerable individual variation in the effective dosage. When the drug is used alone, the best results appear to be obtained if therapy is started the day before exposure to motion. Divided doses seem preferable, and very few individuals have shown undesirable symptoms when 155 milligrammes have been taken with breakfast and 155 milligrammes with the evening meal. Taking V-12 with a meal appears to be desirable, presumably because absorption is prolonged. Resistant individuals may take an extra dose of 155 milligrammes with the midday meal. Therapy should continue during short trips, but the duration of protection after the drug is stopped is probably fifteen to eighteen hours. The immediate symptom of overdosage is sleepiness, and this symptom should be used in assessing the tolerance of the individual. In some cases this may be a desirable feature, but it should definitely contraindicate any increase in dose. In no case should a total of more than 460 milligrammes a day be used, and when such dose is required it should be reduced after one or two days. If prolonged therapy is necessary, it should be realized that thiobarbiturates may cause liver damage, fever and agranulocytosis; any impairment of liver function is a contraindication to the use of V-12.

The outcome of this work was a decision to recommend to the Canadian Armed Services the use of the following mixture dispensed in capsules: hyoscine hydrobromide 0·1 milligramme, hyoscyamine hydrobromide 0·3 milligramme, ethyl β-methyl allyl thiobarbituric acid (V-12) 130 milligrammes. This mixture has been termed the Canadian Motion Sickness Remedy—National Research Council Formula. The dose suggested is two capsules taken two to four hours before exposure to motion. Further treatment should be one capsule every eight to twelve hours. Individuals who are very susceptible to motion sickness may receive increased benefit if therapy is started twenty-four hours before exposure to motion. Undue hypnosis, dryness of the mouth or other untoward symptoms should be promptly followed by reduction in dosage. In no case should more than three capsules be taken within twenty-four hours. For small adults or children the dosage should be reduced. To prevent undue accumulation of the thiobarbiturate, treatment should never be given for more than five days each week. It is interesting to note in passing that a degree of protection (of the order of 20% to 30%) was obtained during the tests by the administration of a placebo; the psychological factor in motion sickness is apparently very powerful. However, the protection afforded by the drugs was very much greater. It is felt that this work is authoritative and likely to be of general application. These wartime findings applied in peace should help to bring physiological peace to those whose bodies war within themselves on shipboard.

[1] *The Canadian Medical Association Journal*, April, 1947.

HYPEREMESIS GRAVIDARUM.

THE assessment of any form of treatment for vomiting during pregnancy is difficult because of the psychological factors involved in the condition and because of the frequent occurrence of spontaneous remission or recovery. The distinction (if any) between simple "morning sickness" and *hyperemesis gravidarum* is still not clearly defined. However, from the practical angle, nausea and vomiting during pregnancy present a worrying problem to both doctor and patient and a reliable and effective form of treatment would be welcome. W. N. Kemp has again brought forward claims for the specific value of adrenal cortex extract[1] based on clinical and endocrinological studies. He states that during the first three months of pregnancy large quantities of chorionic gonadotropin are secreted by the chorionic placenta as part of the mechanism of establishing and maintaining the gestation till the placenta commences to produce progesterone in abundance. When the blood titre of chorionic gonadotropin drops, "morning sickness" usually ceases. Kemp further states that the adrenal cortex undergoes hypertrophy in the first three months of pregnancy "presumably for the purpose of secreting extra cortin necessary for the hepatic detoxication of the excessive quantity of gonadotropin present in the blood stream". When the latter is extremely high a condition of relative cortico-adrenal insufficiency may exist, the excess of gonadotropin causing, as a toxic manifestation, "morning

[1] *The Canadian Medical Association Journal*, April, 1947.

sickness". Normal cortico-adrenal function, according to Kemp, depends upon the presence of at least two vitamins, cevitamic and pantothenic acids. "With increasing nausea and vomiting a vicious circle effect of cortico-adrenal and vitamin deficiency occurs which, if not checked, leads to the so-called pernicious vomiting of pregnancy." Kemp has been publishing the results of treatment based on this conception since 1932 and has apparently achieved satisfactory clinical results. He quotes confirmatory reports from a number of other workers. Two papers in particular are of interest. W. Freeman, J. M. Melick and D. K. McClusky[1] published their results from the treatment with suprarenal cortical extract of 79 patients suffering from vomiting associated with pregnancy; they apparently achieved a high degree of success. A report by J. Kotz and A. B. Kaufman[2] on the results of the treatment of fifty patients was rather more conservative, but they seemed convinced that, allowing for all factors and giving due credit to other elements in the system of treatment adopted, they had to attribute the results essentially to the specific therapy with adrenal cortical extract.

Kemp's recommended regimen is as follows. At bedtime the patient is given a dose of three to ten grains of desiccated adrenal cortex with ten grains of calcium pantothenate and a glass of hot lemonade, or cold orange or tomato juice. This is repeated when the patient awakens next morning; she must then remain in bed in a recumbent position for ninety minutes, when she may have a cup of tea (with sugar, but without milk) before assuming the upright position. Breakfast should consist only of a glass of orange, tomato or grape fruit juice, one slice of lightly buttered toast with marmalade, one or two cups of coffee (without cream, but with milk if desired). Luncheon and dinner are to be normal meals, but preceded by a glass of tomato, orange or grape fruit juice or lemonade. If any symptoms of nausea supervene the nocturnal dose of suprarenal cortex should be increased and a suitable dose of the same preparation should be ingested before breakfast, lunch and dinner.

This form of treatment does not appear to have attracted very wide attention, but its advocates seem strongly convinced of its value after prolonged clinical trial. They also report absence of any obvious undesirable side-effects. Other recent workers have tended to stress the importance of the administration of specific vitamins, especially those of the vitamin *B* complex. In view of the great distress caused by nausea and vomiting during pregnancy, Kemp's recommendations seem worthy of more extensive clinical trial.

WHAT TO DO IN CASE OF VENOUS AIR EMBOLISM.

VENOUS (or pulmonary) air embolism is a rather uncommon occurrence; but it is a most alarming one and often fatal. Air may enter the systemic veins in sufficient quanity to produce serious embolic effects in the course of a number of different surgical procedures: such are operations in which large veins of the head or neck may be opened, and diagnostic procedures in which air is injected, as when gas or air is insufflated through the uterine tubes to test their patency, or round the kidneys for X-ray examination of the suprarenal glands. There is a similar danger during vaginal insufflation with a powder blower and during obstetrical operations in which a hand is introduced into the uterus, also during various other less common surgical manœuvres. It is a not uncommon cause of death during attempts to procure abortion by injections of foreign substance into the uterus with a syringe.

T. M. Durant, of Philadelphia, and his collaborators have made experimental studies of venous air embolism in the dog.[3] Under anæsthesia air was injected intravenously during the experiments, and in some of the animals the thorax was laid open so that the heart could be observed. It was found that a quite large quantity of air might enter a vein without causing serious trouble, provided that it did not enter too rapidly. This is very different from what happens with arterial air embolism, in which very serious peripheral effects may be caused by a minute bubble of air. It appeared also from the experiments that it is possible for a certain amount of air entering the veins to be transported to the lungs and there to be excreted from the circulation, a process accompanied by tachypnœa. When death occurs from venous air embolism, it is due to circulatory obstruction resulting from an air lock in the path of outflow from the right ventricle. The right ventricle in this region becomes dilated and ischæmic. It is in this connexion that the authors have made their most important discovery. If the animal is turned onto its left side, the air forming the lock floats away from the outflow tract and takes up another position. Forceful contractions of the right ventricle are very quickly resumed and the pulmonary circulation is restored; the air in the ventricle is presumably churned into a froth which gradually passes out into the lungs where the air is excreted from the blood stream.

This work of Durant and his collaborators should be applicable to man; if it is, we now possess a logical form of treatment, capable of immediate application and with dramatic effect, for a catastrophe that hitherto placed the sufferer in imminent peril of death. No longer need precious moments be wasted on injections of analeptics or of stimulants for a heart that is doing all it can. The patient will be turned onto the left side.

[1] *The American Journal of Obstetrics and Gynecology*, April, 1937.
[2] *Ibidem*, March, 1940.
[3] *American Heart Journal*, March, 1947.

THE PREVENTION OF TETANUS

IMMUNIZATION with tetanus toxoid, referred to in these columns on January 25, 1941, achieved striking success during the recent war, but little subsequent publicity. Frank Glenn[1] states that the absence of clinical tetanus among United States troops in the South-West Pacific Area attracted little attention until approximately 500 cases of tetanus occurred amongst civilian casualties in the battle for the recapture of Manila in 1945. During the siege tetanus was observed as early as three and as late as twenty days after the infliction of a wound. Severe local tetanus in the vicinity of wounds was observed, and also tetanus of the muscles of the affected extremity. Cephalic tetanus was not seen. Late operative treatment gave disappointing results; while those patients whose condition was good enough for surgery were benefited by it as regards sepsis, they still followed the common pattern of tetanus and died. However, when amputations were performed on patients not showing symptoms of tetanus, the disease rarely developed later, despite its prevalence. Penicillin was used locally and systemically without effect on the tetanus. Little antitoxin was available for specific treatment. The most important single agent for treatment was morphine, which reduced the duration and severity of the spasms, giving the patients rest and enabling those with dysphagia to swallow liquids. A small amount of "Avertin" was available and gave gratifying relief. Of approximately 12,000 civilians wounded, some 473 developed tetanus (about 40 per 1,000) with a mortality of 82%. As far as is known none had been injected with tetanus toxoid before injury. During the decade before the war there was in Manila an annual incidence of tetanus of 75 to 100 cases. This incidence rose during the occupation. Glenn points out that the American soldier fought over the same terrain, yet no cases of tetanus occurred among the United States army forces on Luzon. The military personnel had been treated with tetanus toxoid; also in their favour was their better physical condition, and the fact that they received timely and efficient surgical care. It is surprising that tetanus toxoid has not found more favour in the civilian sphere. Tetanus is not common, but it still occurs when least expected and can still bring death in a horrible form. It should be possible to abolish it completely.

[1] *Annals of Surgery*, December, 1946.

Abstracts from Medical Literature.

SURGERY.

Fall in Blood Pressure during Intrathoracic Operations.

W. H. BILFELDT-NICHOLLS AND A. E. BAWDEN (*The Journal of Thoracic Surgery*, December, 1946) conclude from experiments with dogs that, notwithstanding the findings of L. O'Shaughnessy, the pulmonary plexus plays no part in the sudden fall of blood pressure that may occur during intrathoracic operations, so that infiltration of the hilus with an anæsthetic solution is not necessary. These authors think it more likely that the alterations in blood pressure are due to impediment to the flow of blood into the heart. Such procedures as packing the pleural cavity or excessive pulling during difficult dissections can produce kinking or compression of the great veins and consequently fall in blood pressure.

Autopsy Service at the Mary Hitchcock Memorial Hospital.

RALPH E. MILLER (*The New England Journal of Surgery*, January 23, 1947) states that the Mary Hitchcock Memorial Hospital obtains permission for post-mortem examination in a consistently high percentage of cases—between 80% and 90%—by the adoption of a programme. The essential features of this programme are: (i) a hospital staff that agrees that all deaths be followed by a request for a post-mortem examination; (ii) a department of pathology ready to perform an autopsy at any hour of the day or night required by circumstances; (iii) a public that is informed concerning the value of autopsy; (iv) a cooperative group of funeral directors. It is noted that a final complete report is sent to the family physician to whom the relatives are referred following an interview with the hospital staff. The continuity of the programme is maintained by presenting to each new member of the staff the following statement: "Autopsy percentage will be considered satisfactory when it reaches 100 per cent. Autopsies are done only after permission of the nearest relative or responsible person has been obtained, preferably by interview. It is important that relatives be aware of the following features of the autopsy service. 1. Autopsies are made without charge at considerable expense to give all concerned valuable information not otherwise obtainable. 2. Autopsies are done discreetly in such a manner as to avoid disfigurement of the body so far as the funeral is concerned. The method of autopsy makes better embalming possible for a competent embalmer. 3. Relatives should be assured that autopsy does not necessitate delay."

Care of the Patient Before and After Operation.

OWEN H. WANGENSTEEN (*The New England Journal of Medicine*, January 23, 1947) discusses this subject under three headings: Preparation of the Surgeon, Preparation of the Dissection and Preparation of the Patient. Under the third heading, dealing with the "poor-risk patient", he stresses the importance of careful consideration of four items: water requirements, electrolyte needs, loss of blood, and caloric and nitrogen requirements. The author strongly advocates the use of the weighing scale as an instrument to determine with accuracy the degree of dehydration. He states that it is superior to other procedures in ascertaining early departure from the normal state of hydration of patients during the post-operative period. The method can be carried out to a degree of accuracy of within 100 grammes. As regards blood loss estimation, he recommends the use of dry sponges which are weighed during operation. The gain in weight of the sponges, passed back to be counted by the nurse, is calculated as blood loss. In replacing fluid losses, he advocates that the rule should be to "replace in kind and in amount".

Shunt or By-Pass Operations in Certain Circulatory Disorders.

ALFRED BLALOCK (*Annals of Surgery*, February, 1947) first makes a few general remarks concerning blood vessel anastomosis, particularly in relation to the pressure on the two sides of the union, the technique of the anastomosis and whether it is end-to-end or side-to-side anastomosis. In the management of portal congestion, he considers that anastomosis of the divided distal end of the portal vein to the side of the inferior *vena cava* is a sound procedure. He points out that porta-caval shunt operations are still in the experimental stages, but that it does not appear that the principle of this procedure in the treatment of intrahepatic and extrahepatic block with ascites and gastro-intestinal bleeding is a much sounder one than those previously advocated. The author then mentions a few miscellaneous conditions in which the shunt or by-pass operation may be indicated. He discusses in detail the operation in relation to pulmonic stenosis or atresia. The author and his associates have operated on 243 patients thought to have the "tetralogy of Fallot" with an over-all mortality rate of 9% among the second 100 patients in whom an anastomosis between the end of the subclavian artery and the side of the pulmonary artery was performed. The follow-up periods are considered to be of too short a duration to allow evaluation of final results; however, many of the children appear to be normal, cardiac enlargement after the first several weeks is not progressive and infection with *Streptococcus viridans* has not developed.

Carotid Body Tumours.

H. M. GOLDBERG (*The British Journal of Surgery*, January, 1947) reports two cases of carotid body tumours, and discusses certain aspects of this condition. The carotid body forms part of the chromaffin system and develops from the mesoderm of the third branchial arch; it receives branches from the vagus and the sympathetic. Inconstant in man, the body is usually situated behind the bifurcation of the carotid artery, and measures up to seven millimetres in its long axis. Extirpation or absence of the bodies seems to have no effect, but recent work suggests that they respond to changes in the composition of the arterial blood, decreased oxygen tension and raised acidity causing a rise in cardiac and respiratory rates. Tumours constitute the only pathological condition of the carotid body. They are usually slow-growing and at first benign, but may later become malignant. The diagnosis is seldom made before operation, but once the tumour is exposed, the situation and the extreme vascularity should enable the nature of the condition to be recognized. The detailed structure of the tumours varies; most are peritheliomata, but a few are of nerve-cell origin. The most frequent history is of a painless, slowly growing tumour on one side of the neck. Rarely the tumour is sensitive to touch, but never painful. Hoarseness, dyspnœa, dysphagia, cough, tinnitus from pressure on the vagus, and Horner's syndrome from involvement of the sympathetic are infrequently encountered. In five of the 260 cases in the literature, and in one of the two cases reported by the author, there was associated with carotid body tumour an overactive carotid sinus. The author suggests that the effect may be reflex or due to direct pressure. The tumours are rounded or ovoid in shape, lying partly under the sternomastoid and at the level of the carotid bifurcation. The consistency is firm and the tumour may be moved from side to side but not vertically. Some decrease in size may be noted when the common carotid artery is compressed proximally. Treatment is by surgery, and an endeavour should be made to remove the tumour without ligating the carotid vessels. If ligation is performed the risk of hemiplegia is considerable, and may follow even in young patients. Repeated temporary digital compression of the common trunk during the two or three weeks prior to operation may favour the establishment of a collateral circulation. Radiotherapy appears to be without effect on carotid body tumours.

Treatment of Deep Venous Thrombosis.

WILLIAM D. HOLDEN (*Archives of Surgery*, February, 1947) presents a plan for the treatment of venous thrombosis embracing the physiological principles underlying the use of and the indications for anticoagulant therapy, venous ligation and anæsthesia of the paravertebral sympathetic system. The past ten years have awakened interest in the therapy of deep venous thrombosis. The object of this therapy is to prevent the occurrence of pulmonary emboli and to minimize the late effects of venous obstruction. The author discusses the salient features of paravertebral shock, venous ligation and anticoagulants, and states that of 37 patients treated, 31 received heparin and "Dicumarol" subcutaneously. Of these 31, five underwent ligation of the superficial femoral vein and three underwent paravertebral block for persistent arteriospasm in addition to the administration of the anticoagulants. Sixteen of the 31 patients had pulmonary infarcts when the diagnosis of peripheral venous thrombosis was made. All 31 patients recovered. The author states that when the diagnosis of venous thrombosis is made, an evaluation of the extent and location of the thrombotic process is carried out. If the process is clinically confined to the popliteal and calf veins, bilateral ligation of the superficial femoral vein is immediately performed with the patient under either local or intravenous "Pentothal Sodium" anæsthesia, according to the general condition of the patient. Whether ligation is performed

or not, 300 to 400 milligrammes of a preparation of heparin in Pitkin menstruum are given subcutaneously after the clotting time has been determined, provided that there is no contra-indication to anticoagulant therapy. (Pitkin menstruum consists of gelatin 15% to 30%, dextrose 5% to 12%, glacial acetic acid 0·5%, and sufficient distilled water to make 100%.) If the operation has been performed, this preparation is given at its termination. After the prothrombin clotting time has been determined 300 milligrammes of "Dicumarol" are given. Determination of the base level of the prothrombin clotting time is especially necessary in diabetic, malnourished and elderly patients, those suffering from cardiac disease, and those recently operated on. If the initial level is below 100% of the normal, modified doses of "Dicumarol" are administered. No anticoagulants are given to patients with any hæmorrhagic disease or hepatic or renal insufficiency, or to those with a history of a recently bleeding peptic ulcer, or to patients immediately before or after parturition. When anticoagulants are used, heparin should be given subcutaneously immediately. Prolongation of the clotting time is effected within one or two hours. The use of "Dicumarol" alone without heparin is not justified, since the effect of "Dicumarol" is not apparent for forty-eight hours. Blocking of the lumbar sympathetic chain is used if the pain in the extremities is not relieved within forty-eight hours after anticoagulant therapy is started.

Vitallium Tubes in Biliary Surgery.

HERMAN E. PEARSE (*Annals of Surgery*, December, 1946) discusses the results which have been obtained by the use of vitallium tubes in the repair of the bile passages. Pearse introduced the method in 1940, and has recently written to other surgeons in an attempt to ascertain their experiences. From replies received, and from his own practice, Pearse was able to assemble a series of 229 cases. In 106 cases vitallium tubes had been used to repair a damaged or excised common duct. Good results were reported in 80·1% of cases, which compares very favourably with series treated by other methods. However, in twelve cases (11·3%) the results were described as poor, the tube having become plugged. This complication is one which cannot easily be remedied. Analysis shows that the plug contains from 36% to 56% of cholesterol, the remainder of the plug being insoluble and consisting mainly of bile pigment and calcium. One hopeful aspect has come to light. In two instances in which the author removed a tube which had become plugged (after two years and three and a half years respectively) it was found that the lining mucosa of the duct appeared to have regenerated and presented a normal appearance; favourable progress followed removal of the tube without replacement. In 79 instances a hepatico-duodenostomy was performed over a vitallium tube, with a report of good results in some 58% of cases. Pearse does not approve of this method, and, where the lower end of the common duct cannot be located, recommends that the proximal bile duct be anastomosed to a portion of bowel not containing food. This is best done by dividing the jejunum, bringing up the distal end for hepatico-jejunostomy, and restoring the alimentary continuity by an anastomosis-*en-Y*. Of the eighteen cases in which some form of hepatico-jejunostomy had been performed, results were good in 83%. Three cases were reported in which vitallium tubes were used to anastomose the pancreatic duct to the intestine, with satisfactory results.

Needle Biopsy in Tumour Diagnosis.

FRANK ELLIS (*The British Journal of Surgery*, January, 1947) discusses his experiences with needle biopsy of tumours in over 900 cases over a period of eight years. After stressing the advantage of confirming a clinical diagnosis by histological investigation, especially where the results of treatment by radiotherapy are to be evaluated, the author refers briefly to the views of other workers concerning the method, and lists the circumstances in which needle biopsy is especially indicated. These include cases in which the usual methods of obtaining histological material are contraindicated or in which a major operation would be necessary for this purpose and would still not allow of successful extirpation of the tumour. The results of the method were "useful" in approximately two-thirds of the cases in which it was employed. The material obtained is small in size, but is much better than no material at all. The author carries out aspiration biopsy using an ordinary syringe and needle, or drill biopsy. In the latter method a trocar and cannula are used, the edge of the cannula's end being sharpened. When the cannula has entered the tumour the trocar is removed and the cannula rotated and advanced, a plug of tissue being cored out.

Two Hundred and Thirty-Six Lobectomies with One Death.

R. H. MEADE *et alii* (*The Journal of Thoracic Surgery*, February, 1947) describe 236 consecutive operations for pulmonary lobectomy with only one death, the fourth patient of the series.

Congenital Dislocation of the Hip.

M. BECKETT HOWORTH (*Annals of Surgery*, February, 1947) dissected the hip joints of fifteen fœtuses ranging in fœtal age between ten weeks and full term. None of these specimens showed a congenital dislocation. However, the author has examined at operation more than 100 hips showing congenital dislocation, and his article is based on these examinations and about 200 open operations and 50 shelf stabilization operations. He describes the anatomy and development of the fœtal hip, the evolution of the anteversion and the tension of the capsule and the pathology of congenital dislocation of the hip. He states that congenital dislocations of the hip should be reduced as soon as possible after they are recognized, as the results are more favourable in proportion to the earliness of the age of the patient. Closed reduction is the treatment of choice for infants if it can be accomplished with little trauma. Open reduction should be used for infants older than eight months if closed manipulations fail and for all older children when there is any possibility of securing a movable stable hip. When open operation fails or is inadvisable, the shelf stabilization operation or vitallium cup arthroplasty should be used in selected cases or an arthrodesis performed. The results of the surgical treatment of congenital dislocation of the hip are very favourable when there is careful selection of the type of treatment, due regard for operative technique and avoidance of trauma, and proper after-care.

Total Gastrectomy.

FRANCES H. SMITH (*Surgery, Gynecology and Obstetrics*, April, 1947) reviews 89 cases of total gastrectomy performed at the Lahey Clinic between 1927 and 1945. The indication was usually neoplastic disease, but two gastrectomies were performed for chronic gastritis and one for multiple ulcers. The post-operative mortality for the entire group was 29%, but for the last 43 cases this fell to 16%. Twelve patients have survived the operation for three years or more. Smith discusses the causes of death, both before and after discharge from hospital, and presents a plan for post-operative nutritional care by which it is claimed the patient will eventually be able to maintain weight and strength on three meals per day.

Certain Pelvic Tumours Associated with Ascites and Hydrothorax.

ACCORDING to Marvin Calmenson, Malcolm B. Dockerty and John J. Bianco (*Surgery, Gynecology and Obstetrics*, February, 1947), the association of ascites and hydrothorax with pelvic tumours was described in the older medical literature, but remained comparatively unknown to most of the medical profession until Meigs's classical report in 1937. The greatest credit is due to Meigs for recognizing this syndrome and pointing out its clinical importance. A condition once thought to be an inoperable malignant process is now amenable to complete surgical cure. Meigs's syndrome originally was described as the coexistence of ascites and hydrothorax with benign fibroma of the ovary. Other pelvic tumours, however, both benign and malignant, should be included in the syndrome because they are being reported in the literature with increasing frequency. Nine cases of pelvic tumour associated with ascites and hydrothorax were found in the records of the Mayo Clinic. In a tenth case the patient was seen at that clinic after the authors' paper had been completed. The nine reports included those of five ovarian fibromata, one degenerating uterine fibromyoma, one fibromyoma of the uterus with pelvic inflammatory disease of the adnexæ, one granulosa-cell tumour of the ovary, and one complex teratoma of the ovary. In the tenth case the lesions were ovarian fibromata. Pathologically, all the tumours were of the solid variety and were large, averaging sixteen centimetres in diameter. Gross œdema of the tumour was noted in each of the ten specimens. Microscopically, intercellular œdema was noted in each tumour. It would seem that this œdema can be correlated with the clinical production of ascites in each case. A large solid tumour can readily produce partial venous obstruction, œdema and, in turn, ascites. Partial obstruction to the venous return also may result from twisting of a pedicle, inflammation, or adhesions. In eight of the ten cases, hydrothorax was situated on the right side. It was bilateral in one case and had occurred on the left side in one case. On the basis of the evidence reviewed, it appears that the fluid in the thorax results from the passage of ascitic fluid through the diaphragmatic lymphatic vessels.

Bibliography of Scientific and Industrial Reports.[1]

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken from former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 425, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) The reports referenced with an E number may be obtained in approved cases without cost on application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

PB 40369. YOUNG, GEORGE A., JUNIOR, *et alii*. Respiratory pathogenicity of *Bacillus anthracis* spores: I. Methods of study and observations on pathogenesis. No date. 32 pp. Price: Microfilm, $1.00; Photostat, $3.00.

An exposure method for producing experimental respiratory anthrax in several species of animals is described. This exposure technique *plus* statistical treatment of the resulting data makes possible quantitative comparison of the relative pathogenicity of different anthrax spore suspensions and of the comparative susceptibility of animal species. A description of the histopathology of respiratory anthrax is given. From the essentially negative pathology it is pointed out that anthrax produced by inhalation of anthrax spores is not a specific disease of the lungs but rather a systemic disease. The invasion of the host by inhaled anthrax spores is shown to occur through the lymphatic system. Quantitative studies made on the organisms present in the lungs and peribronchial lymph nodes indicate that highly pathogenic spores are more invasive than spores of moderate respiratory pathogenicity. A diagram of the respiratory exposure chamber and tables are included, together with a bibliography. This work was carried out at Camp Detrick, Frederick, Maryland.

E 648. LOVELACE, W. R. Research in aviation medicine for the German Air Force. (Research in Aviation Medicine.) (C.I.O.S. File No. XXVI-56.) 83 pp. Varied reports on research work and problems, mainly concerned with flying personnel.

The above report (referenced with an "E" number) may be obtained by approved applicants without cost from the Secondary Industries Division of the Ministry of Post-War Reconstruction, 203, Collins Street, Melbourne, C.1. Copies are available also for reference in public libraries.

PB 40370. ZELLE, M. R., *et alii*. Respiratory pathogenicity of *Bacillus anthracis* spores: II. Genetic variation in respiratory pathogenicity and invasiveness of colonial variants of *Bacillus anthracis*. 1946. 20 pp. Price: Microfilm, $1.00; Photostat, $2.00.

Four colonial variants of *Bacillus anthracis* were found to vary significantly in respiratory pathogenicity for guinea-pigs and rats. No significant differences between the four variant types were observed in subcutaneous virulence tests on guinea-pigs and mice, but significant differences were observed in subcutaneous virulence for rats. Significant differences in the ability of the four types to invade through the tissues of the lungs were demonstrated. It appeared that fatal respiratory infections with *Bacillus anthracis* resulted from effective invasion by only a very few spores. Significant differences in respiratory pathogenicity were observed between cultures of the same colony type. Tables and bibliography are included. This work was carried out at Camp Detrick, Frederick, Maryland.

PB 40974. CHAMBERS, ROBERT. Micromanipulative studies of capillaries in relation to shock. Progress Report, Nos. 1-15. February, 1942, to December, 1943. 36 pp. Price: Microfilm, $1.00; Photostat, $3.00.

Various phases of the study of shock are summarized in these progress reports. The following subjects are included in the study: microscopic observations of the capillary bed; the capillary bed during peripheral circulatory failure; experimentally induced hæmorrhage in the rat; Collip-Noble method of inducing shock; toxic effect of shock blood; changes in the perfusion fluid on passage through the vascular bed of a frog's leg; depressor action of serum from shocked animals; surface-chemical studies on corticosteroids; pitressin therapy; analysis of factors leading to the irreversible phase in dogs subjected to graded hæmorrhage; the predisposing action of anæsthetics on the development of so-called irreversibility and on that of vaso-depressor factors during the hæmorrhagic shock syndrome in the dog. A few tables of data are included; a number of the pages are not duplicated well. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract No. OEMcmr-3).

PB 40984. CLARK, WILLIAM G., *et alii*. Chemotherapy. Surgical infections. Monthly Progress Report, No. 2. July, 1943. 19 pp. Price: Microfilm, $1.00; Photostat, $2.00.

This progress report deals with the following topics: (1) studies of substances which enhance sulphonamide bacteriostasis in the presence or absence of sulphonamide inhibitors; (2) topical chemotherapy of staphylococcic dermal wounds in rabbits; (3) chemotherapy of experimental gas gangrene; (4) studies of agents claimed to accelerate wound healing, including observations on burn films; (5) clinical observations. This report was prepared under the auspices of the Committee of Medical Research, Office of Scientific Research and Development.

PB 40359. FINE, JACOB W. Shock. Progress Report, Nos. 5-26. July, 1942, to October, 1945. 55 pp. Price: Microfilm, $2.00; Photostat, $4.00.

These progress reports describe various phases of the study of hæmorrhagic shock. By means of radioactive salts information was obtained regarding the movement of plasma and plasma protein in shock. The blood contents of the peripheral tissue, capillaries and various organs of the body were determined by the same means. The reports record the results of the use of various substances such as hypertensin, bovine albumin, succinic acid, pitressin (vasopressin) and ergotamine, paredrine (*p*-(2-aminopropyl) phenol or *p*-hydroxy-α-methylphenylethyl-amine) and sodium chloride for the attempted therapy of irreversible shock. The reports also investigate the following: intermediary metabolism of hæmorrhagic shock, blood viscosity and cardiac output; liver perfusion in shock; vivi-perfusion of the liver after the development of irreversible shock; peritoneal dialysis for the treatment of uræmia; use of cytochrome C in shock. These progress reports cover work done under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract No. OEMcmr-21).

PB 41055. RICHARDS, DICKINSON W., JUNIOR. Shock. Monthly Progress Report, Nos. 1-23. April, 1942, to June, 1945. 57 pp. Price: Microfilm, $2.00; Photostat, $4.00.

A study of various types of shock was made. Most of the subjects were patients who had been admitted to the emergency ward of Bellevue Hospital, New York City. A description of the subjects is included in the reports. Tables record the various measurements and observations made. These tables include the effects of adrenal cortical extracts; *influence of pressor amines, including methedrine (N,α-*dimethylphenethylamine); influence of alcoholism upon various hæmodynamic measurements. Some pages will not *reproduce well. These reports covered work performed under* the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract *Nos. M-912 and OEMcmr-107). Another investigator in this* work was André Cournand.

PB 41053. FLEXNER, L. B., AND GELLHORN, A. Traumatic *shock. Monthly Progress Report, Nos. 1-3 and 5-11. May,* 1942, to June, 1943. 15 pp. Price: Microfilm, $1.00; Photostat, $1.00.

These progress reports summarize the testing of the transfer of radioactive sodium in the blood stream of traumatically

[1] Supplied by the Information Service of the Council for Scientific and Industrial Research.

shocked dogs by venous injection of $Na^{24}Cl$. Experiments showed that the proportion of total sodium leaving the blood stream was greater in shocked animals than in normal dogs. This permeability, even with a depressed blood pressure, was higher than in the control animals. Other experiments showed that the increased rate of equilibrium was not peculiar to sodium, but could be produced by other ions and that this was due to the altered capillary physiology in traumatic shock. It was also seen that the rate of equilibration of intravenously injected radioactive sodium proceeds at a double exponential rate in both the normal and the shocked dog. Tests showed that in shock produced by muscle crushing, there is a decreased rate of exchange of sodium across the vascular membrane. Several tables are included. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract No. OEMcmr-115). Another investigator often mentioned is George W. Corner.

PB 42493. U.S. CLIMATIC RESEARCH LABORATORY, LAWRENCE, MASS. Long-term acclimatization to heat. June, 1946. 10 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This report presents data relating to the physiological response of seven healthy males to daily exposure in conditions of high temperature and humidity during an extended period. The subjects, after being acclimatized for one month, were exposed to these ambient conditions for six months. The results indicate that there is no trend in either the pulse rates or rectal temperatures. However, five of the seven subjects exhibited a decline in sweat rate throughout the experimental period. The implications of these observations are briefly considered. Tables and graphs are included.

PB 47070. BODENSTEIN, DIETRICH. Investigations on the reproductive system of Drosophila. No date. 63 pp. Price: Microfilm, $2.00; Photostat, $5.00.

Certain aspects in the development of the reproductive system of Drosophila were investigated by means of transplantation and extirpation experiments. The following are some of the findings: (1) pupal ovaries of two-day-old melanogaster and three-day-old virilis are able to develop to maturity when transplanted into adult hosts; (2) ovaries of decapitated newly emerged melanogaster flies can develop a few mature eggs while the ovaries of decapitated virilis remain immature; (3) transplantation of extra ovaries brings about reduction in the size of the host ovaries, while extirpation of one ovary results in an increase in the size of the remaining ovary; (4) adult immature ovaries will mature in either a larval or pupal environment; (5) ovaries of mature larvæ transplanted into adult hosts are unable to develop, but stay alive without further differentation; (6) transplantation of larval ring glands or *corpora allata* into young adult flies accelerates the maturation of the ovary; (7) transplantation of extra ovaries had no effect on the *corpus allatum* of the host; (8) transplantation of extra *corpora allata* into newly emerged flies caused the host *corpus allatum* to atrophy; (9) larval testes, in contrast to larval ovaries, are able to continue their development when transplanted into adult hosts; (10) the larval ring gland loses its ability to promote growth of larval disks within two days after pupation; (11) certain larval disks are able to develop in adult male flies only in the presence of larval ring glands, while in female adults they will develop even without the support of the ring glands. Tables, photographs, diagrams and bibliography are included. This report is a contribution from the Medical Division, Edgewood Arsenal, Maryland.

PB 40966. CATTELL, MCKEEN, AND GOLD, HARRY. The pharmacology of BAL. February, 1943. 33 pp. Price: Microfilm, $1.00; Photostat, $3.00.

The physiological effect of small and large doses of BAL (1,2-dithioglycerine) on cats was studied. The study included symptoms, effect on blood and urine, lethal dose, anatomical and histological changes, excretion of BAL, effect on circulation, and action on smooth muscle. The effect of injections of lactic acid and of Compound "139" was also noted. Tables and graphs, together with a bibliography, are included. The report covers work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-245).

PB 40928. CALVERY, HERBERT O., *et alii*. An investigation into the biological properties of BAL solutions and ointments and of new compounds which may be developed as useful substitutes for BAL. Progress Report, Nos. 1-8. April, 1943, to March, 1944. 99 pp. Price: Microfilm, $2.00; Photostat, $7.00.

Modifications of laboratory methods for the application of M-1 (Lewisite) and for the evaluation of the results are described. Also studied are the factors relating to exposure of M-1 and the effects of the concentration of BAL or the related compounds employed. The effect of these agents when applied to the eyes and skin of animals and also when injected are noted. So also are the systemic effects of the compounds. A summary of pharmacological findings is included in the reports. The reports also cover the following topics: effectiveness of BAL derivatives; comparison of ointments of different strength; effect of modifications of ointments or solutions; deterioration of BAL; comparative efficiency of New York Conference ointments in treatment of M-1 skin burns on rabbits. Several diagrams, tables and graphs are included. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contracts M-2214 and M-2760).

PB 40926. CALVERY, HERBERT O., *et alii*. The protective action of BAL in acute antimony intoxication. Supplementary Report, Nos. 1-2. July to December, 1944. 4 pp. Price: Microfilm, $1.00; Photostat, $1.00.

The effect of BAL in acute antimony intoxication in rabbits was investigated. Three antimony compounds were employed: (1) antimony tartrate; (2) a trivalent antimonial, "Fouadin"; a pentavalent antimonial, "Neostam". The results are tabulated. BAL was found to have a protective action in the rabbit against acutely toxic doses of the antimony compounds tested. Supplementary Report 2 describes a test to determine the antidotal action of BAL on chromates. As in the previous experiment, the rabbit was used. A table records the results. The data indicate that BAL has a protective action in cases of poisoning with chromates at the toxic dose of potassium chromate, namely, 15 milligrammes per kilogram. At higher doses, however, BAL is not as effective as it was in the case of arsenic and antimony, where it protected in some cases against more than one and a half times the fatal dose. BAL, however, is ineffective in chromate poisoning if applied after renal damage has occurred. These reports are supplementary to the reports covered by *PB 40928*. These reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contracts *M-2214* and *M-2760*).

PB 40979. CHARGAFF, ERWIN. Typhus vaccine. Progress Report, Nos. 1-17. October, 1942, to June, 1945. 43 pp. Price: Microfilm, $1.00; Photostat, $3.00.

A study was made of the chemical and immunological properties of specific fractions isolated from epidemic rickettsiæ which were grown in infected chick embryos. The vaccine fractions include the supernatant, diethylene glycol extract, tryptic digest (fast and slow electrophoretic fractions, nucleic acid). Data on the soluble antigens from yolk-sacs infected with epidemic and endemic rickettsiæ are also included. Because of the well-known agglutinability of certain Proteus strains by typhus sera, the experimental work was extended to a study of the chemical and serological properties of fractions obtained from *Proteus vulgaris* OX-19. The material used consisted of the washed formolized organisms which were dried by lyophilization. In order to obtain comparable results, the methods of extraction and isolation of the various fractions follow closely those employed in the study of the composition of epidemic rickettsiæ. Tables record the serological activity of the fractions. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-228).

PB 40990. COBB, STANLEY, AND MORRISON, L. RAYMOND. Effect of Anoxia upon nerve cells. Progress Report, Nos. 1-18. February, 1942, to June, 1944. 20 pp. Price: Microfilm, $1.00; Photostat, $2.00.

In these experiments dogs have been exposed to atmospheres low in oxygen. The exposures were usually three or four hours long and occurred daily except Sunday. They ranged from one exposure at an atmosphere at 2·5% oxygen to about 35 or more exposures at 13%. The animals were unable to live in the 2·5% oxygen, but when 4% oxygen or more was available, they survived for varying lengths of time indefinitely. No untoward clinical signs were observed in the richer atmospheres. Studies on arterial blood consisting of O_2 and CO_2 hæmatocrit and sugar were made on these animals. Histological studies on the central nervous system, the splanchnic nerves and the adrenals were likewise made. The chief lesions in the brain were found in animals exposed to the lower oxygen atmospheres. Dogs exposed to 13% atmospheres showed no lesions. These histological alterations in the brain were virtually identical with lesions in six out of nine monkey brains that had been chronically exposed to low oxygen in a decompression chamber. Mild alterations were observed in the adrenals and splanchnic nerves of the dogs. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-30).

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on April 17, 1947, at the Royal Alexandra Hospital for Children. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. Parts of this report appeared in the issues of July 12 and 26, 1947.

Congenital Cystic Disease of the Lung.

DR. T. Y. NELSON presented a girl, aged eight years, who had had cough with sputum since the age of four and a half years following tonsillectomy. An X-ray examination in March, 1947, had revealed extensive saccular bronchiectasis and considerable atelectasis involving almost the whole of the lower lobe of the left lung. The right side of the chest appeared normal. In April, 1947, the lower lobe of the left lung was removed. Continuous suction of the chest was employed post-operatively. On April 8, 1947, the child had developed pneumonia which was resistant to penicillin but responded to sulphadiazine. The pathologist's report on the specimen of lung removed at operation was as follows:

> Left lower lobe of lung: Oblique cut taken to pass through a large cyst which was evident to external inspection on the lower medial border. The cut surface revealed that the bronchi were dilated and had thickened walls. In addition there were a number of cysts with a thick opaque lining; these communicated with the bronchial tree. Much of the pulmonary parenchyma surrounding the bronchi was consolidated, firm and grey. The cyst at the lower medial border differed from those present elsewhere, in that it was larger (1·5 and 2·7 centimetres), thin-walled and lined by a smooth membrane. No communication could be established between this cyst and the bronchial tree. Sections taken from many parts to include thickened dilated bronchi, saccular bronchial dilations (communicating cysts), consolidating pulmonary tissue and the wall of the large basal cyst. These sections all revealed gross inflammatory damage to the bronchi; eosinophiles were fairly numerous in the granulation tissue which replaced the bronchial walls. The intervening lung tissue showed a varying picture of collapse, consolidation and fibrosis. The large cyst was lined by a single layer of tall columnar epithelium which rested upon a layer of fibrous tissue in which there were a small number of chronic inflammatory cells and eosinophile leucocytes.
>
> Diagnosis: Saccular bronchiectasis.
>
> Comment: There is no convincing evidence of any congenital abnormality of the bronchi as a basis for the lesion. Though the large smooth-walled cyst does not communicate with the bronchial tree, it seems most reasonable to assume that it represents merely a variant of the other cysts present and differs from these because it has been cut off from the bronchial tree by fibrosis.

Foreign Body in Duodenum.

DR. L. G. TAIT presented a girl, aged eighteen months, who had swallowed a two and a half inch sewing needle on February 17, 1947. The needle had apparently passed into the duodenum within one or two days and had stayed in the descending portion of the duodenal loop. It was removed from this position on April 2, 1947. At operation a part of the needle was found to be protruding through the duodenal wall, and a small tube was left in the abdomen for four days. The child had made an uneventful recovery. Dr. Tait considered that probably the laparotomy should have been performed much sooner, but as the child seemed to have no discomfort whatever it had been hoped that the needle would pass on.

Vaginal Anus.

Dr. Tait's next patient was a girl, aged nine years, who had been first admitted to hospital when four years of age. At that time she had had no control of fæces, she suffered from constipation and abdominal distension and was subject to infection of the urinary tract with *Bacillus coli communis*. Ombredanne's operation had been performed without preliminary colostomy. The basis of this operation was the making of two transverse incisions: an anterior one for separating the rectum from the vagina and a posterior one for implanting the rectum into the perineum. The operation had been unsuccessful; the anal opening returned to the vagina. Four years later, in December, 1946, inguinal colostomy had been performed. In January, 1947, a medial perineal incision had been made and the rectum separated from the vagina. The posterior wall of the vagina had been sutured; the perineal tissues between the rectum and vagina had been firmly united with catgut, and the opening of the rectum placed in the normal position of the anus. In March, 1947, the colostomy wound had been closed. The child was much more comfortable; she was not constipated and was able to arrange her toilet better.

DR. C. H. WESLEY presented an infant who had been admitted to hospital on February 4, 1947, at the age of one day, with a vaginal anus. The infant had been discharged the following day after the anus had been dilated with Hegar's dilators. The anus was to be dilated once a week.

Imperforate Anus.

Dr. Wesley's next patient was a boy, aged eleven months. He had been admitted to hospital on May 23, 1946, at the age of one hour, with imperforate anus, bifid scrotum and hypospadias. An operation had been performed on the imperforate anus, an incision being made through to the anal canal. The rest of the condition had not been interfered with surgically. The child had been discharged on June 10, 1946, and was having regular dilatation of the anus with Hegar's dilators.

DR. J. STEIGRAD presented an infant suffering from imperforate anus. A blind rectal pouch was present, but there was no anal dimple or fistula. X-ray examination had been made by the Wangensteen and Rice method in which the child was inverted by the legs and an opaque disk placed in the position of the anus. This method gave information of practical value twelve hours after birth, after the child had swallowed air. The X-ray examination revealed about three centimetres of tissue intervening between the rectum and the perineal skin. For this reason the operation of left inguinal colostomy was performed, the child being one day old. It was proposed that, when the child was twelve months old, a rectoplasty operation would be undertaken.

Acute Osteomyelitis.

Dr. Steigrad then presented a series of patients illustrating the value of treatment of acute osteomyelitis with penicillin. The first patient was a boy, aged seven years, who had been admitted to hospital in September, 1946. He had been kicked on the right wrist about five days before admission and had had, since the injury, increasing pain and swelling extending from the wrist to the elbow. On admission he was found to be gravely ill and delirious, with a temperature of 104° F. The right forearm was œdematous and extremely tender, and a blood culture revealed the presence of *Staphylococcus aureus*. He was given morphine and the arm splinted in the position of function. Penicillin was administered intramuscularly (50,000 units every three hours for five doses, 20,000 units every three hours for eighteen doses), then hypodermically (20,000 units every six hours for ten doses); the total dosage was 4,750,000 units during a period of four weeks. Tenderness had persisted for two weeks, but the condition had completely responded without surgical interference. The child was discharged from hospital on October 28, 1946.

The next patient was a boy, aged seven years, who had been admitted to hospital on January 15, 1947, having been kicked above the left knee one week previously. At the time there had been a furuncle of the left ear. He had been ill for three days prior to admission. The illness had commenced with shivering, fever and headache; on the following day he had complained of pain in the left thigh and calf, this rapidly becoming worse; he had been vomiting. On admission he was found to be very ill, dehydrated and delirious; his temperature was 104° to 105° F. Extreme tenderness was present in the region of the lower third of the left femur on all aspects. A blood count revealed 17,800 leucocytes per cubic millimetre, of which 18% were neutrophile cells; the hæmoglobin value was 12 grammes *per centum*. Incubation of the blood failed to reveal any pathogenic organisms. The boy was treated with morphine and splintage, and penicillin was administered intramuscularly (50,000 units every three hours for four doses, then 25,000 units every three hours) to a total dosage of 4,750,000 units in a period of three weeks. The condition had responded to the penicillin and the patient was discharged from hospital on February 7, 1947, wearing a splint, with instructions that he was to stay in bed.

Dr. Steigrad's third patient was a girl, aged six years, who had been admitted to hospital on January 15, 1947, with a history that she had been limping for five days prior to admission with increasing pain in the right ankle; there had been no history of trauma. On admission the patient's

temperature was normal; she was pale and ill, but her constitutional upset was not as marked as in the case of the two preceding patients. There was marked tenderness and œdema of the right ankle and the lower end of the right tibia. A blood count revealed the presence of 18,200 leucocytes per cubic millimetre, of which 75% were neutrophile cells. The child was given morphine, and a long leg and foot splint was applied. Penicillin was administered intramuscularly, 60,000 units being the initial dose and then 25,000 units at intervals of three hours; the total dose was 5,250,000 units during a period of three weeks. After four days' treatment the child was still pale and ill and showing no improvement. She had complete anorexia, and local swelling with slight fluctuation was present over the lower end of the right tibia. An incision was made and a subperiosteal abscess was opened; this was not packed, and no tubes were necessary. Incubation of the pus yielded *Staphylococcus aureus* sensitive to penicillin, one-sixteenth of a unit per millilitre. Healing was complete in three or four weeks. A plaster of Paris cast had been applied to the leg and the child spent one month at Collaroy.

The fourth patient presented by Dr. Steigrad was a girl, aged ten years, who had been admitted to hospital in September, 1946, having been treated for five weeks prior to admission. The onset of her illness had been accompanied by pain and high fever and a diagnosis of rheumatism was made. The child had then developed a local abscess which was incised and continued to discharge. She had received sulphanilamide, but no penicillin. On admission to hospital her temperature was normal and had remained so. A discharging sinus was present above the left medial malleolus. X-ray examination showed the presence of osteomyelitis in this area with a sequestrum. The foot was fixed in full plantar flexion. *Staphylococcus aureus* was grown from the wound; it was sensitive to penicillin, one thirty-second of a unit per millilitre. Treatment adopted consisted of removal of the sequestrum and the administration of penicillin, 15,000 units being given intramuscularly at three-hourly intervals for eighteen days and then 20,000 units hypodermically for ten days, a total dosage of 2,750,000 units during a period of twenty-eight days. In addition gradual daily stretching of the *tendo Achillis* had been carried out. The wound had healed in four weeks, and the child was discharged from hospital after fourteen weeks, wearing a walking caliper.

Pigmented Nævus of Face and Head.

Dr. Steigrad's last patient was a girl who had been admitted to hospital in 1942 with an extensive pigmented nævus extending over the right half of the forehead down to the right cheek and including the right upper and lower eyelids, and upwards about three inches into the hair line. Operation was commenced in July, 1942, by raising a tube graft on the abdominal wall; this was then transferred via the right forearm to the forehead. In January, 1943, the nævus was dissected up from before backwards; the tube graft was opened and spread on the facial and anterior part of the bed thus made. The posterior part of the nævus remained. In 1943 to 1944 a further tube graft was raised on the abdomen and transferred to the scalp via the right forearm. The remainder of the nævus was excised and the graft spread over the area. In March, 1947, the nævus was excised from around the right eye and a free skin graft from the right arm was sutured over the bare area.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Prince Alfred Hospital on May 22, 1947. The meeting took the form of a series of clinical demonstrations by members of the honorary and resident medical staff of the hospital.

Besnier-Boeck's Disease.

DR. T. M. GREENAWAY presented an example of the condition known as Besnier-Boeck's disease, sometimes referred to as sarcoidosis and again as Besnier-Boeck-Schumann disease. The patient had presented, some eighteen months previously, swollen glands in the right groin which were first of all thought to be the result of an infection in her foot. They did not subside, however, and several months later persistent cough resulted in her having an X-ray examination of her lungs. The film which was submitted showed the typical nodular appearance of sarcoidosis and the diagnosis was confirmed by gland biopsy. A slide showing the typical histological appearance was also submitted. Over the course of the previous few months glandular swellings had made their appearance in the other groin and in both axillæ. The glandular swellings had subsided dramatically with deep X-ray therapy, though the pulmonary condition appeared to be at the same stage. The patient, however, had gained weight and was subjectively very well.

Adenoma of the Islets of Langerhans.

Dr. Greenaway then demonstrated two patients in whom the surgical removal of adenoma of the islets of Langerhans had resulted in apparent cure of their symptoms. These patients had both had recurrent episodes of drowsiness, even coma, which were relieved by the administration of glucose. Blood sugar contents in both cases, the patient being in the fasting state, had been at the extremely low levels of 30 milligrammes *per centum* and 40 milligrammes *per centum*. The varying symptomatology of the condition known as hyperinsulinism was referred to and the triad postulated by Whipple for the diagnosis of insulin adenoma was stressed, namely: (i) recurrent episodes affecting the central nervous system and occasionally the alimentary tract, (ii) relief with glucose administration, (iii) a fasting blood sugar level of below 50 milligrammes *per centum*.

Another patient was also presented who gave a somewhat similar history including two epileptiform seizures which occurred in the early hours of the morning. The fasting blood sugar contents were variable, on some occasions being normal, but on at least two occasions being below 50 milligrammes *per centum*. This patient differed from the other two demonstrated in that she had also complained for a year or more prior to admission to hospital of a dull pain towards the left side of the abdomen extending into the back. After consultation with Dr. B. T. Edye, exploratory operation was decided upon, but no insulin adenoma could be found. The operation of hemipancreatectomy was performed, the pancreas being removed from the tail up to the site of crossing of the superior mesenteric vessels. The patient made an uninterrupted recovery and had been completely free from symptoms ever since operation, a period of two years.

Unipolar Electrocardiography.

DR. KEMPSON MADDOX demonstrated the wiring of a patient for the taking of the unipolar electrocardiogram, using the Wilson central terminal connected to one pole of the electrocardiograph, the other pole becoming the exploring electrode. He also demonstrated a multiple switch by means of which standard limb leads, unipolar limb leads, and all chest leads could be obtained without changing the limb electrodes. He explained that the advantages of the unipolar technique were: (*a*) greater accuracy; (*b*) ability to determine the true electrical axis of the heart, and to assess the influence of this axis upon the conformation of the standard limb leads; (*c*) ability to observe the reflection upon certain limbs of known aspects of the free ventricular surfaces; (*d*) exact diagnosis of ventricular hypertrophy, partial and complete bundle branch block; (*e*) precise localization in site, depth, and lateral extent of myocardial infarcts. His remarks were illustrated by a series of diagrams and by unipolar electrocardiograms prepared by the electrocardiographic department of the Royal Prince Alfred Hospital.

Chronic Endocarditis with Pulmonary Diastolic Murmur.

DR. J. H. HALLIDAY showed a female patient, aged twenty-three years, who had been admitted to the Royal Prince Alfred Hospital on April 17, 1947, very distressed and cyanosed, with a history of abdominal pain and increasing breathlessness during the preceding three weeks. She was found to be febrile, and there were signs of consolidation at both lung bases. She was given penicillin and sulphadiazine. Her temperature rapidly subsided, and her general condition quickly improved. Her previous history was that during childhood she had had measles, whooping-cough and numerous sore throats, and tonsillectomy had been performed at the age of twelve years. In recent years she had become increasingly breathless on effort, and this had become more pronounced during pregnancy three years previously; at the end of pregnancy she had had a very stormy labour. She stated that she had not suffered from acute rheumatism; this was confirmed by her mother. The salient points on physical examination were the presence of cyanosis of the lips with some malar flush, but no clubbing of the fingers and cardiac enlargement particularly to the left of the sternum in the pulmonary region where a definite thrill was present in the second interspace; at the mitral area there were variable presystolic and constant systolic murmurs, and at the pulmonary area a loud and prolonged diastolic murmur replacing the second sound. The blood pressure was 120 millimetres of mercury (systolic) and 80 millimetres of mercury (diastolic). The electrocardiogram showed right ventricular preponderance with accentuated *P* waves indicating auricular enlargement. The teleröntgenogram

was reported on as follows: "Congestive changes throughout both lung fields, especially the pulmonary arteries. The configuration of the heart conforms to a mitral stenosis, and on screening with a barium bolus the left auricle appeared to be considerably enlarged. One could not entirely exclude some congenital abnormality as well."

Dr. Halliday's comment was that the patient was presented as a diastolic problem, with the uncommon physical sign of a very pronounced pulmonary diastolic murmur. Lutembacher in 1915 had described the association of mitral stenosis with a defect of the interauricular septum. In this condition, however, the right auricle enlarged, the left auricle remained small, and the basal murmur was usually systolic in time. He considered that the patient might present an example of congenital idiopathic dilatation of the pulmonary artery with mitral stenosis; the cardiac silhouette tended to support this view. Otherwise the patient might present an example of the Graham Steele murmur associated with mitral stenosis, and secondary incompetence of the pulmonary valve associated with high pulmonary pressure.

Patent Interventricular Septum (Maladie de Roger) with Complete Heart Block.

Dr. Halliday's second patient was a boy, aged five years, who was the second child in a family of three. His mother had been quite well during pregnancy and there had been no history of rubella. The boy's cardiac murmur was first discovered when he entered hospital in 1945 with an attack of scarlet fever. He was a very active boy, always "on the go". No abnormal physical signs were present except in relation to his heart. On examination the heart was enlarged to the left, and a systolic murmur was present over the whole of the precordium, of maximal intensity in the second and third left intercostal spaces adjacent to the sternum. At times the auricular sound was heard by itself, and at other times reinforcing the first sound at the mitral area. The blood pressure was 100 millimetres of mercury (systolic) and 70 millimetres (diastolic). The electrocardiogram showed complete auriculo-ventricular dissociation (auricular rate, 100 per minute; ventricular rate, 55 per minute). The report of X-ray findings was as follows: "There is well-marked general enlargement of the heart. There is some venous congestion of the lungs and a rather strong pulsation was noted in the pulmonary conus and pulmonary vessels. The X-ray appearance strongly suggests a congenital defect in the heart probably with interventricular septal defect."

Dr. Halliday commented that Roger's original description in 1879 of this congenital defect was still adequate. It was revealed only on auscultation by a physical sign with very definite characters; this was a long loud murmur. It began in systole and was prolonged to such an extent as entirely to cover the natural tic tac of the heart sounds. It had a maximum intensity not at the apex, but over the upper third of the precordial region. It was chiefly medial in position like the septum itself, and from this central position it diminished in intensity uniformly as one moved the stethoscope over the chest. The murmur was not transmitted to the vessels. It coincided with no other sign of heart disease except a harsh thrill which accompanied it. This murmur was the pathognomonic sign of an interventricular septal defect.

The presence of complete heart block in association with this common congenital cardiac abnormality was most unusual, and very few cases had been reported in the literature.

Neurological Case for Diagnosis.

DR. C. R. BICKERTON BLACKBURN showed a patient with neurological signs and symptoms for diagnosis. The patient, who was a man of forty-nine years and a wireworker by occupation, had presented at the out-patient department on January 3, 1947. He stated that he had noticed an aching pain in his left arm, particularly in the triceps region, in the middle of November, 1946. Within five to six days of the onset of this pain his arm was "paralysed" from the elbow to the hand. During this period of five to six days he noted some numbness and tingling of his hand and fingers, and this was most marked on the radial side. There were no other symptoms or signs of any kind; he specifically stated that there was no febrile illness, and he had had no recent attack of "influenza". There was no relevant family or past history. He had had no exposure to industrial noxious agents. On examination the only abnormalities found related to the nervous system, and these were confined to the left upper extremity. There was gross atrophy of the *biceps brachialis*, of all the muscles of the forearm except the *flexor carpi ulnaris*, and of all the small muscles of the hand except the *interossei* and *adductor pollicis*. No fibrillation or fasciculation had ever been noted. The triceps reflex on the left side was normal, but neither biceps nor wrist reflex could be elicited. Sensory changes were limited to the periphery of the extremity; there was hypoæsthesia to all superficial forms of sensation over the dorsal aspect of the hand and wrist, extending medially as far as the middle finger, and similar findings were recorded on the palmar aspect of the hand. Appreciation of a vibrating tuning fork appeared to be normal. The left hand was œdematous, and this was related to the dependent position, for it was rapidly relieved by using a sling; the finger nails were cyanotic and this, together with the œdema, produced an effect similar to the *main succulente* of syringomyelia. The electrical reactions of the affected muscles were as follows: to faradism, no reaction; to galvanism, sluggish reactions of all muscles to twenty milliamperes. Examination of the rest of this extremity and of the remainder of the body showed no abnormality. Lumbar puncture revealed clear cerebro-spinal fluid under a pressure of 70 millimetres of water; there was no increase in the number of white blood cells; the total protein content was 20 milligrammes per 100 millilitres, and there was no increase in the amount of globulin present; the Wassermann test produced negative findings; the Lange curve was "1100000000". The results of blood Wassermann and Kline tests were negative. Radiological examination revealed no osseous cervical rib and the lung fields appeared to be normal. Dr. Blackburn then discussed the patient's progress. With physiotherapy the patient considered that he had improved. Objectively there had been a considerable increase in strength in the unaffected muscles, but little change was apparent in the atrophic muscles. The sensory changes had disappeared, the last signs being present some three months after the onset of the condition. General examination of the patient revealed no other changes since he had first presented. Dr. Blackburn considered that the diagnosis lay between poliomyelitis with unusually prolonged sensory changes and, as suggested by Dr. K. B. Noad, brachial neuritis.

Apical Pulmonary Carcinoma with Hypertrophic Osteoarthropathy.

DR. MAURICE JOSEPH presented a male patient, aged fifty-eight years, who had been admitted to hospital on October 14, 1946. The patient had been well until eighteen months previously, when, after doing some home carpentry, he had noticed that his knees were swollen. A few weeks later the ankles and wrists had become enlarged. These changes only occasioned slight discomfort and he continued with his work. Six months later he developed pain in the chest, beneath the left scapula and below the left clavicle, which was aggravated by coughing. He had had a cough with scanty sputum for many years and did not notice any increase in its severity at this time. His only other symptoms at the time of admission were lack of energy and some loss of weight. He had suffered from pleurisy in 1936. When examined on admission to hospital his temperature was 100° F., his pulse rate 96 per minute and his respiration rate 24 per minute. He had considerable enlargement of the hands and feet with clubbing of fingers and toes. The appearance resembled acromegaly except for the absence of prognathism. The joints of the hands, feet, wrists and ankles were swollen but not tender. The soft parts of the extremities were thickened but there was no pitting œdema. Dulness to percussion and diminished air entry were found at the apex of the left lung. The pulse was regular, the blood pressure was 160 millimetres of mercury (systolic) and 100 millimetres (diastolic). The apex beat was in the fifth intercostal space in the mid-clavicular line. No abnormality of the nervous system was found except slight weakness of the left leg.

On November 17, 1946, unilateral sweating of the left arm sufficient to saturate the pyjama sleeve was noticed for the first time. This continued for approximately five weeks. On December 15, 1946, the patient complained of severe pain radiating down the left arm with signs of paresis of the ulnar and median nerves. On January 2, 1947, drooping of the left eyelid was noticed, and on January 5 the patient had a complete left-sided Horner's syndrome. Repeated examination of the sputum by direct smear, culture and guinea-pig injection failed to reveal the presence of *Mycobacterium tuberculosis*. The following was the report of findings on X-ray examination of the chest and extremities on November 10, 1946: "There is some consolidation in the extreme left apex with thickening of the overlying pleura and there is some patchy consolidation in the right upper lobe. While somewhat atypical, I think the lesion is probably an old very chronic type of pulmonary tuberculosis. There is slight general enlargement of the heart. Over the distal end of the right femur and over the metacarpals and to a lesser extent over the phalanges there is well-marked periosteal reaction due to hypertrophic pulmonary osteoarthropathy. The pituitary fossa appears normal." On

January 16 the radiologist reported: "There is a mass in the left apex. There is no evidence of rib destruction yet, but the appearance suggests a superior sulcus tumour." On February 19 he reported: "There is periosteal thickening of the metatarsal bones and the proximal phalanges. Appearances are those of hypertrophic pulmonary osteoarthropathy." Bronchoscopic examination and bronchograms revealed no bronchial obstruction. Blood counts showed a mild secondary anæmia and leucocytosis. Owing to the obvious nerve involvement, operation was considered impracticable and a course of deep X-ray therapy was given to the tumour and to the left hand to see whether it would influence the osteophytosis. There had been some reduction in the swelling of the soft tissues of the hands and feet, but no change in the radiographic appearances of the bones. The pain in the left upper extremity had continued unabated and the hand had become useless. Horner's syndrome (drooping of upper lid, myosis, enophthalmos and anidrosis) was fully developed. The signs in the chest (diminished movement on the left side, dull percussion note over the upper lobe and weak or absent breath sounds) had become more pronounced, probably owing in part to fibrosis induced by X-ray therapy. Dr. Joseph considered that the case was of interest, firstly because the patient had presented with arthritic symptoms, and secondly because the ætiology of hypertrophic osteoarthropathy (Marie-Bamberger's disease, generalized osteophytosis) was still obscure. Craig (*British Medical Journal*, April 10, 1937) had reported four cases of pulmonary neoplasm in which hypertrophic osteoarthropathy was the first symptom. Three patients were treated as suffering from rheumatoid arthritis and one was sent to Queen's Square Hospital as a case of acromegaly. Compere and Adams (*Surgery, Gynecology and Obstetrics*, Volume LXI, Number 3, 1935, page 312) presented an experimental and clinical study of the disease with X-ray and autopsy findings showing marked periosteal new bone formation. They were unable to produce the condition experimentally. Campbell (*British Medical Journal*, Volume I, 1924, page 145) claimed that hypertrophic osteoarthropathy was an advanced grade of the Hippocratic fingers and that in all cases the essential feature was a chronic anoxia which led to œdema of the soft tissues of the terminal phalanges where the circulation was slowest and later to periosteal stimulation. However, clubbing of the fingers even in marked degree was seen so commonly and hypertrophic osteoarthropathy was so rare that Dr. Joseph thought that there must be an essential difference between the two. Moreover, in osteoarthropathy the "clubbing" was different from that seen in the Hippocratic fingers, in that it was not of the drumstick or bulbous type.

Congenital Syphilis.

DR. ERIC SUSMAN presented a female patient, aged twenty-one years, who had come to the hospital in May, 1947, complaining of progressively failing vision for five years. Ophthalmic examination in 1942 had revealed early optic atrophy, and the result of the Wassermann test was positive. No other symptoms were noted. The patient's mother gave a positive reaction to the Wassermann test; there was, however, no history of primary infection or of secondary manifestations, and, apart from an ulcer of the leg in 1946 which might have been of varicose origin, she was completely asymptomatic. The patient's father and two younger sisters had negative serum findings. The maternal grandfather related that his wife had been suffering from syphilis, but he, as well as the patient's aunts and uncles on the maternal side, gave a negative response to serological tests. Dr. Susman stated that specific interrogation had revealed that the patient had been a frail baby, very slow to develop, and had suffered from some indefinite malformation of her ankles in childhood. On examination, the patient was rather under-developed for her age; some frontal bossing of the skull was present; rhagades were seen at the angles of the mouth; the upper teeth were false, the lower teeth peg-shaped. Atrophy of both optic nerve heads was well marked. No other abnormality was detected on careful examination of the central nervous, cardio-vascular and respiratory systems, or of the abdomen. The results of blood Wassermann and Kline precipitation tests were positive. The cerebro-spinal fluid contained ten cells per cubic millimetre, 90% of which were lymphocytes and 10% mononuclear and polymorphonuclear cells. The fluid had a protein content of 35 milligrammes *per centum* and an increased globulin content. A positive result was obtained from a Wassermann test on the fluid and the Lange colloidal gold test gave the following curve: 4433100000. The blood contained 13·3 grammes of hæmoglobin *per centum* (91% of normal); the total number of white cells was 8,850, of which 74% were neutrophile cells, 20% lymphocytes and 6% monocytes. Dr. Susman said that it was intended to inoculate the patient with malarial blood and to give her an intensive course of penicillin coincidently, with the hope of arresting the further progress of the disease.

Reifenstein-Klinefelter-Albright Syndrome.

Dr. Susman next presented a patient suffering from the Reifenstein-Klinefelter-Albright syndrome. The patient, a male, aged forty-three years, had been complaining of sore and swollen legs and feet for the previous nine months; his ankles and feet assumed a purplish colour when dependent, and he experienced a burning sensation in them a short while after assuming the erect posture. Lately his hands had been similarly affected. He had been suffering from neurasthenia for twelve years, and had been receiving a pension for this. He was listless, not very interested in his surroundings, and unable to read or write, mainly because he could not be bothered to learn. He had been impotent for twenty years, had no libido, and was unable to have an erection, but claimed that he had infrequent nocturnal emissions. Apart from mumps at the age of seven, nothing relevant was reported in his past health. His family history and personal environment contained nothing of significance. On examination the patient was found to be very tall, lean, and of eunuchoidal proportions as follows: total height, six feet five and a half inches; vertex to coccyx, three feet one inch; tip of greater trochanter to sole, three feet six and a half inches; acromion to finger tips, two feet seven inches; span, six feet four inches. His skin was soft, smooth and thin; no hairs were present on his limbs or trunk. The pubic hair was scanty and of female distribution. He always appeared clean-shaven, though he shaved only once a week. There was no gynæcomastia. The penis was rather smaller than was normal. Two small, flat, ovoid testicles, each measuring three-quarters of an inch by half an inch, could be palpated in the scrotum; testicular sensation was present in these. Both ankles and feet were tender to palpation; they became deeply congested after being dependent for one minute, but soon blanched again on elevation. The arteries of both lower limbs appeared normal to palpation. No other significant abnormality was detected on careful examination of the central nervous, cardio-vascular and respiratory systems and of the abdomen. Biopsy from the right testicle revealed aspermatogenesis, atrophy and hyalinization of the seminiferous tubules and hyperplasia of the interstitial cells of Leydig. Examination for 17-ketosteroids revealed 1·5 milligrammes in a twenty-four hour specimen of urine. In the investigation for urinary gonadotropins, a concentrate of one litre of urine produced a *corpus luteum* in the ovary of one immature female mouse. The basal metabolic rate was −11%. The sugar tolerance curve was within normal limits. X-ray examination of the *sella turcica* revealed no abnormality. Blood Wassermann and Kline tests gave negative results. The blood contained 14·0 grammes of hæmoglobin *per centum* (96%) and the total number of white cells was 11,200 per cubic millimetre, of which the differential count was normal. Dr. Susman considered that the clinical, histological and biochemical findings brought the patient within the syndrome described. It was intended to institute testosterone therapy.

Penetrating Gastric Ulcer.

DR. F. W. NIESCHE showed a male patient, aged forty years, who had been suffering from a high penetrating gastric ulcer on the lesser curvature and posterior wall which had been treated by subtotal gastrectomy. When this patient had first come under medical care he had had abdominal discomfort and dyspepsia for seven to eight years; this had been persistent for the previous twelve months. Pain had been present in the left hypochondrium continually for the previous year with more severe exacerbations. It awakened him at night after about two hours' sleep. Food relieved him for about one hour and then pain returned. Flatulence and acid regurgitations were troublesome. Vomiting had recently become frequent. Pain was increased when he lay on the right side. Hæmatemesis, melena or jaundice had not occurred. He smoked about four cigarettes per day. He had lost two stone in weight since June, 1945. The report on X-ray examination was as follows: "There is a large penetrating ulcer on the lesser curvature of the stomach at the junction of the upper and middle thirds with marked hour-glass deformity. Some delay is present in the upper pouch. The stomach is not freely mobile." Medical treatment had given him no relief. He had been admitted to a surgical ward on January 10, 1947. Pain in the left epigastrium was then almost continuous throughout the day. At night the pain awakened him about two hours after he had gone to sleep. The taking of food did not ease his pain, but he was relieved somewhat by alkaline powders. Flatulence and regurgitation of food occurred and he vomited small amounts

every second or third day. On examination his tongue was clean and moist. No palpable masses were detected in the abdomen. Tenderness was present in the region of the umbilicus and left epigastrium with some muscle guarding. Examination by a fractional test meal showed a high climbing acid curve. His blood pressure measured 115 millimetres of mercury (systolic) and 90 millimetres of mercury (diastolic). The hæmoglobin value of his blood was 62%. On February 24 laparotomy was performed through an upper mid-line incision. Extensive adhesions were present. The lesser curvature of the stomach was grossly adherent to the left lobe of the liver. On separation of adhesions the large ulcer became detached from the left lobe, revealing an extragastric pocket in the liver about the size of a golf ball. On account of soiling the ulcer was oversewn and a rubber tube put down into the cavity in the liver through a stab wound. On March 31 an incision was made through the old mid-line scar with a left transverse extension. Formidable adhesions were encountered and separated. The stomach was mobilized and a large ulcer crater penetrating the pancreas exposed. This was completely separated round the margins, the base was undisturbed. Subtotal gastrectomy was performed with difficulty. An antecolic, retroperistaltic anastomosis was performed. The pathologist's report on the tissue removed was as follows: "A large gap in the lesser curvature has been formed by ulceration. The stomach wall on each side is thick and œdematous. Diagnosis—chronic peptic ulcer—no evidence of malignancy. A large gland removed showed sinus catarrh—no malignancy." Convalescence was reasonably uneventful. A week following operation the patient had some pain in the chest. Examination of the blood showed low coagulation time and he was given a prophylactic dose of heparin. At the time of the meeting he was very well, increasing in weight and symptomless.

Dr. Niesche's next patient was a male, aged forty-three years, who had had a high penetrating ulcer on the lesser curvature of the stomach with hour-glass deformity and who had been treated by subtotal gastrectomy. He had been admitted to hospital on February 27, 1947, with a history of epigastric pain after meals for ten years. He had been treated for a duodenal ulcer for some years. Seven years previously he had been operated upon for a perforated ulcer. Until four months before admission his condition had been relatively quiescent, provided that he kept up a diet *régime*. In November, 1946, he had had a severe hæmatemesis and had had four attacks since. He had required blood transfusions for these. He had lost some weight. He was a heavy smoker, but took no alcohol. On examination he looked older than his stated age and appeared underweight. His abdomen showed a scar of a previous operation. Some tenderness and muscle guarding were present in the epigastrium, but no other abnormalities were palpable. His blood had a hæmoglobin value of 63%. Examination by a fractional test meal showed a high climbing acid curve. The report on X-ray examination was as follows: "Penetrating ulcer on the lesser curvature of the stomach at junction of upper and middle third with some irregularity of the lesser curvature above. Hour-glass deformity. Suggestive of malignancy." His blood hæmoglobin value was raised to normal pre-operatively. On March 12, 1947, operation was performed under anæsthesia with cyclopropane and curare. A right paramedian incision was made and extensive adhesions were separated with difficulty. A large penetrating ulcer was present, high on the lesser curvature and posterior wall with marked hour-glass deformity. After the duodenum was severed and oversewn, the stomach was mobilized and a very large ulcer separated from the pancreas, the base of the ulcer being left undisturbed. The stomach was freed above the ulcer and a subtotal gastrectomy performed, an antecolic and retroperistaltic anastomosis being made with the jejunum. The condition of the patient on return to the ward was good. Three days later he was seized with sudden substernal pain. This was followed by slight hæmoptysis. Both saphenous veins were thrombosed. A blood coagulation chart was begun. X-ray examination subsequently showed a pulmonary infarction at the base of the right lung. He was treated with heparin until his coagulation time was within normal limits. His convalescence subsequently was uneventful. He was very well at the time of the meeting and had no symptoms.

Carcinoma of the Hepatic Flexure of the Colon.

The last patient shown by Dr. Niesche was a female, aged sixty-five years, suffering from carcinoma of the hepatic flexure of the colon, of which the presenting symptoms had been marked loss of weight, tiredness, loss of appetite and a functioning caecostomy. She had been quite well until October, 1945, when she was seized with sudden pain in the abdomen, not accompanied by vomiting. Appendicectomy was performed. The patient had continued to have less severe attacks of pain, these being accompanied by vomiting. Loss of weight was over two stone. She had never been subject to constipation. During January, 1946, a caecostomy was performed and this relieved her of her symptoms. In February, 1946, a laparotomy and an ileo-transverse colostomy were performed. Her relatives were told that she had a carcinoma of the hepatic flexure which was inoperable. In April, 1946, an attempt to close the caecostomy failed. At this stage she consulted Dr. Niesche. She was admitted to the Royal Prince Alfred Hospital on August 29, 1946. On examination she was found to be an elderly woman of small build who had obviously lost weight. Her condition was moderately good. Two laparotomy scars were present, one midline and one paramedian. The caecostomy was still discharging. A fairly fixed mass was palpable in the right hypochondrium. X-ray examination indicated the presence of a carcinoma of the hepatic flexure of the colon with a functioning ileo-transverse colostomy. On September 18, 1946, an operation was performed through a right paramedian incision. Adhesions were gross and the viscera were adherent to the abdominal wall. The ileo-transverse colostomy stoma appeared adequate. The caecostomy opening was dissected out and freed and a hemicolectomy was performed. The hepatic flexure was fixed and was mobilized with difficulty, this necessitating the removal of half the gall-bladder, portion of the second part of the duodenum and the capsule of the lower pole of the right kidney. Enlarged glands at the base of the mesentery were removed with the colon. The patient's condition at the end of the operation was good. The pathological report on the tissue removed advised the presence of a mucoid adenocarcinoma with glandular involvement. The patient's convalescence was uneventful. At the time of the meeting her condition (after eight months) was very satisfactory, she felt well and had gained over two stone in weight.

Dr. Nietsche considered that on account of the glandular involvement her ultimate prognosis was doubtful, but that the resection had been worth while.

Aneurysm of the Abdominal Aorta.

DR. N. R. WYNDHAM showed a patient suffering from aneurysm of the abdominal aorta. The patient was a man, aged sixty-five pears, with pain in the hips and inferior extremities, typical of that due to local ischæmia. The principal clinical features were a large pulse pressure, interference with bowel action, and an abdominal tumour at the level of the bifurcation of the aorta. It was possible to feel arterial pulsation in the legs, but this was of poor volume. The blood Wassermann test gave negative results. Calcification of the walls of the tumour was visible by X-ray examination. The tumour was not very expansile.

Autopsy Specimens.

DR. CLEMENT CHAPMAN showed autopsy specimens from three subjects.

The first comprised pelvic hydatid cysts from a woman, aged fifty-six years, who had complained of lower abdominal swelling, epigastric pain and constipation for three years; she had not lived out of Sydney. On examination a largish oval tumour, six inches by four inches, freely movable in the lower part of the abdomen, had been felt, also a cystic swelling three inches in diameter in the right fornix, and a slightly enlarged retroverted uterus with two rounded tumours, each one and a half inches in diameter, on the posterior wall. As the tumour did not feel hard enough for fibromyoma, and had a peculiar doughy feel, hydatids were thought of; a Casoni test was carried out with an inconclusive result. The pre-operative diagnosis was then changed to "multiple fibroids". At operation the tumours were found to be hydatids. The large one had no pedicle and was just a wandering tumour, oval in shape, rambling about the lower part of the abdomen. It was filled with disintegrated hydatid material. There was another cyst in the region of the right ovary also dead. The two smaller cysts were subserous and active, containing live daughter cysts. Subtotal hysterectomy with double salpingo-oophorectomy was performed. No primary cyst was discovered by palpation of the liver or by X-ray examination of the lung.

The second specimen presented by Dr. Chapman was a microscopic slide from the uterus of a married woman, aged fifty-five years. She had had the menopause ten years previously and had suffered from post-menopausal irregular bleeding four years before. Curettage revealing no evidence of cancer, she had had an intrauterine application of radium by experts at another hospital. Following this she had had intermittent hæmorrhage and continuous discharge ever

since. Total hysterectomy and double salpingo-oophorectomy were performed and the report on microscopic examination of the specimen was *"adenomyosis uteri"*. The point of interest, Dr. Chapman considered, was the failure of the radium to cure the bleeding from *adenomyosis uteri*. This patient now had no discharge and no bleeding since her hysterectomy.

Dr. Chapman's third specimen was from a woman, aged thirty-eight years, who had had menorrhagia, vaginal discharge and pelvic pain for three years. On examination she had a hard uterus four inches by three inches by two inches in size, and a *cervix uteri* with chronic erosion. No sign of contact bleeding was seen and no ulcer was detected. Total hysterectomy and double salpingo-oophorectomy were performed for chronic cervicitis and metritis, and for salpingo-oophoritis. Microscopic examination of the cervix revealed a very early squamous carcinoma with typical cell change and commencing invasion. Dr. Chapman pointed out that there were three lessons to be learnt from the case: (*a*) always to examine every patient very carefully in the lithotomy position before proceeding to abdominal section for pelvic disease; (*b*) always to have the removed tissue microscopically examined; (*c*) always to perform total hysterectomy if practicable.

(To be continued.)

NOTICE.

THE General Secretary of the Federal Council of the British Medical Association in Australia has announced that the following medical practitioner has been released from full-time duty with His Majesty's Forces and will resume civil practice as from the date mentioned:

Dr. Kevin Coen, 215, Macquarie Street, Sydney (August 8, 1947).

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

GENERAL PRACTITIONERS' REFRESHER COURSE.

THE Melbourne Permanent Post-Graduate Committee announces the following programme for the General Practitioners' Refresher Course which will be held from September 22 to October 4, 1947.

Monday, September 22.—9 to 11 a.m.: "Eye Conditions in General Practice", Dr. A. S. Anderson, at the College of Surgeons. 2 to 4 p.m.: "Heart Disease in Childhood", Dr. L. Stokes, at the Alfred Hospital.

Tuesday, September 23.—10 a.m. to 12 noon: "Chronic Pulmonary Infections", Dr. G. Penington, at the Royal Melbourne Hospital. 2 to 4 p.m.: "Pain: Its Diagnostic Significance to the Surgeon", Dr. A. E. Coates, at the Royal Melbourne Hospital.

Wednesday, September 24.—10 a.m. to 12 noon: "Urological Problems in General Practice", Dr. H. Mortensen, at Saint Vincent's Hospital. 2 to 4 p.m.: "Vulval Conditions", Dr. L. Gleadell, at the Royal Melbourne Hospital.

Thursday, September 25.—10 a.m. to 12 noon: "Ear, Nose and Throat Problems in General Practice", Dr. E. Gutteridge, at the Eye and Ear Hospital. 2 to 4 p.m.: "Infectious Diseases", Dr. F. V. Scholes, at the Infectious Diseases Hospital, Fairfield.

Friday, September 26.—10 a.m. to 12 noon: "Investigation of the Treatment of Dyspepsia", Dr. J. E. Sewell, at the Alfred Hospital. 2 to 4 p.m.: "Minor Injuries of the Hands", Dr. C. A. Renou, at the Alfred Hospital.

Saturday, September 27.—10 a.m. to 12 noon: "Therapeutics", Dr. B. L. Stanton, at the Royal Melbourne Hospital.

Monday, September 29.—10 a.m. to 12 noon: "Disproportion", Dr. I. Hayes, at the Women's Hospital. 2 to 4 p.m.: "Sterility", Dr. J. W. Johnstone, at the Women's Hospital.

Tuesday, September 30.—10 a.m. to 12 noon.: "Diseases of the Anus", Dr. R. Officer, at the Alfred Hospital. 2 to 4 p.m.: "The Early Diagnosis of Pulmonary Tubercle Bacilli", Dr. E. Clarke, at the Alfred Hospital.

Wednesday, October 1.—10 a.m. to 12 noon: "The Anæmias", Dr. J. Bolton, at the Royal Melbourne Hospital. 2 to 4 p.m.: "Thyreoid Disorders", Dr. E. E. Dunlop, at the Royal Melbourne Hospital.

Thursday, October 2.—10 a.m. to 12 noon: "Heart Diseases", Dr. J. G. Hayden, at Saint Vincent's Hospital. 2 to 4 p.m.: "Insanities Arising during the Puerperium", "Senile Psychoses", Dr. J. K. Adey, at the Royal Park Hospital.

Friday, October 3.—10 a.m. to 12 noon: "Orthopædic Problems in Childhood", Dr. E. Price, at the Children's Hospital. 2 to 4 p.m.: "Some Recent Advances in Pædiatrics", Dr. V. Collins, at the Children's Hospital.

Saturday, October 4.—10 a.m. to 12 noon: "Legal and Ethical Problems in Medical Practice", Dr. C. Dickson, at the Medical Society Hall, Albert Street.

In addition to the subjects arranged, opportunity will be given for discussion on problems submitted by those attending the course. The fee for this course is £10 10s. and the class will be limited to 20. Applications should be made a fortnight before the commencement with the Secretary of the Committee, College of Surgeons, Spring Street, C.1 (JM 1547). The course has been approved under the Commonwealth Reconstruction Training Scheme.

Professor R. W. Gerard, of the University of Chicago, will give evening lectures between September 29 and October 15.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

COURSE IN GYNÆCOLOGY AND OBSTETRICS.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the honorary medical staff of the Royal Prince Alfred Hospital, it will hold a course in gynæcology and obstetrics at the King George V Memorial Hospital for Mothers and Babies, Camperdown, from September 1 to September 12, 1947.

The fee for the course will be £5 5s., and registration is limited to twelve persons. Applications for registration, accompanied by a remittance for the amount of the fee, should be made to the Course Secretary, Post-Graduate Committee in Medicine in the University of Sydney, 131, Macquarie Street, Sydney. Telephones: BW 7483-B 4606.

Gynæcology.

Monday, September 1.—9.30 a.m.: "Ectopic Pregnancy", Dr. G. G. L. Stening. 11 a.m.: "Operative Demonstration", Dr. G. G. L. Stening; "Demonstration in the Use of Curare in Anæsthesia", Dr. W. I. T. Hotten. 2 p.m.: "Therapeutic Aspects of Post-Operative Complications", Dr. M. J. L. Stening. 3.30 p.m.: "Endometriosis", Dr. M. B. McIlrath.

Tuesday, September 2.—9.30 a.m.: "Carcinoma of the Cervix Uteri", Dr. H. H. Schlink. 11 a.m.: Operative Demonstration, Dr. H. H. Schlink, "Wertheim's Panhysterectomy". 2 p.m.: "The Ureter in Gynæcological Surgery", Dr. M. B. Fraser. 3.30 p.m.: Operative Demonstration, Dr. M. B. Fraser.

Wednesday, September 3.—9.30 a.m.: "The Surgery of Prolapse" (colour film), Dr. H. H. Schlink. 11 a.m.: Operative Demonstration, Dr. H. H. Schlink, "Manchester Repair". 2 p.m.: "Gynæcological Pathology", Dr. Mary Heseltine. 3.30 p.m.: "Curare in Gynæcological Surgery", Dr. W. I. T. Hotten.

Thursday, September 4.—9.30 a.m.: "Pelvic Pain and Backache", Dr. G. G. L. Stening. 11 a.m.: "Backward Displacement of the Uterus", Dr. F. N. Chenhall. 2 p.m.: "Ovarian Cysts and Neoplasms", Dr. M. B. Fraser. 3.30 p.m.: "Post-Abortional Sepsis", Dr. Mary Heseltine.

Friday, September 5.—9.30 a.m.: "Progress in Gynæcological Surgery in the Past Twenty Years", Dr. F. N. Chenhall. 11 a.m.: Operative Demonstrations, Dr. F. N. Chenhall, "External Shortening and Total Hysterectomy". 2 p.m.: "Presentation of Selected Cases", Dr. Margaret Mulvey. 3.30 p.m.: "Conservation in Gynæcology", Dr. J. G. Loxton.

Obstetrics.

Monday, September 8.—9.30 a.m.: "Obstetrical Pathology", Dr. Mary Heseltine. 11 a.m.: "News and Views from the International Congress at the Rotunda, Dublin", Professor B. T. Mayes. 2 p.m.: "Ante-Natal Care", Dr. A. F. Hobson. 3.30 p.m.: Symposium, "Diabetes and Pregnancy", Dr. J. Kempson Maddox and honorary obstetricians.

Tuesday, September 9.—9.30 a.m.: "Obstetrical Difficulties", Dr. H. B. Williams. 11 a.m.: Ward rounds, Dr. H. B.

Williams. 2 p.m.: "Hydatidiform Mole: A Clinical Entity", Dr. J. W. Knox. 3.30 p.m.: "Radiology in Obstetrics", Dr. D. G. Maitland.

Wednesday, September 10.—9.30 a.m.: "Post-Partum Hæmorrhage", Dr. W. D. Cunningham. 11 a.m.: Ward rounds, Dr. W. D. Cunningham. 2 p.m.: "The Ætiology of the Toxæmias of Pregnancy", Dr. R. F. Back. 3.30 p.m.: "Breech Presentation" (colour film), Professor B. T. Mayes.

Thursday, September 11.—9.30 a.m.: "The Toxæmias of Pregnancy", Dr. H. B. Williams. 11 a.m.: "Hæmolytic Disease of the Newborn", Dr. Mary Heseltine. 2 p.m.: "Ante-Partum Hæmorrhage", Dr. R. H. Syred. 3.30 p.m.: "Physiology of the Newborn", Dr. S. P. Bellmaine; "Diseases of the Newborn", Dr. N. C. Cunningham.

Friday, September 12.—9.30 a.m.: "Anæsthesia and Analgesia in Obstetrics", Dr. W. D. Cunningham. 11 a.m.: "Lower Segment Cæsarean Section" (colour film), Professor B. T. Mayes. 2 p.m.: "Early Upsets in Pregnancy", Dr. A. F. Hobson. 3.30 p.m.: "Management of the Normal Newborn", Dr. S. P. Bellmaine; "Management of the Premature Baby", Dr. N. C. Cunningham.

Special Correspondence.

CANADA LETTER.

FROM OUR SPECIAL CORRESPONDENT.

A VISIT to New York has brought to our attention the Vanderbilt Clinic, which offers to medical students intensified clinical teaching not available in comparable measure in Canada. In the Group Clinic which functions for special examinations, within the usual out-patient department, patients are first examined and have their histories taken by medical students in their final year. When this is completed, the physician or surgeon in attendance, who is a member of the staff of Columbia University, reviews the case with the student. Specialists who are also members of the Medical Faculty of Columbia University may be called when consultation appears necessary. On return visits the patient is referred to the same student, who thus has the best of opportunities for complete follow-up, under excellent supervision, of all the cases he works up. This would seem to be a great improvement on the clinical teaching methods in most medical schools.

A second discovery in New York was the Tompkins Square House, operated in association with the Department of Welfare of New York, as a home for the aged. It consists of a block of one-roomed and two-roomed apartments accommodating sixty people. Those old people of moderate means who could not afford to live in a commercial establishment, in addition to a few old-age pensioners, are well housed there. A cafeteria is run in the building, towards which each tenant must contribute $15 per month. In addition, kitchenettes are provided—one to each four one-roomed apartments and one to each two two-roomed apartments. Bathrooms are shared on a similar scale. We have been considering in our own mind an application of this plan to provide a place for retired nurses whose savings are, unfortunately, usually very small.

From Saskatchewan comes news of the recruiting among senior high school and undergraduate university students for work in provincial mental hospitals. "Those accepted will be given an intensive three-year training course in psychology to qualify them for psychiatric work in mental hospitals or for instruction in the training school for the mentally retarded." The course is aimed at enabling the students to understand human behaviour and the problems of patients as well as to train mentally retarded people to live in the community as self-supporting citizens.

Dr. John A. Ryle, founder of the Institute of Social Medicine at Oxford University, has been giving a series of lectures in Canada on the relations between sickness and social conditions. He says: "Modern medicine has been giving too much attention to techniques of treatment and laboratory research, but too little to the underlying social causes of bad and good health."

In the May, 1947, issue of *Canada's Health and Welfare*, the feature article is entitled "The X-Ray Goes North on the Nascopie". The *Nascopie* carried medical personnel and supplies on an annual three-month, 10,000-mile voyage north of the sixtieth parallel to the Hudson Bay area, Keewatin and Baffin Land. An extensive survey of the health of Canada's 6,000 Eskimos was commenced on last year's trip. The survey includes a general physical examination and search for tuberculosis, dental care, eye tests and glasses where needed, inoculations, and instructions on proper maternal care and hygiene. Nursing stations are being set up this year at several key points and a comprehensive educational scheme in the field of preventive medicine is being inaugurated.

A few statistics on Eskimo health may be of interest. No cancer or nervous, mental and heart diseases were found. Healed tuberculous bone lesions demonstrated that a degree of immunity to that disease has been built up. The most common cause of death among adults is drowning; 50% of all deaths occur before three years of age. No severe rheumatic conditions were seen, nor were there cases of appendicitis, venereal disease, infected sore throat or tonsillitis. Only 128 natives out of 1,547 examined needed glasses.

Correspondence.

RECENT ADVANCES IN MEDICINE IN ENGLAND.

SIR: I was interested to read in Dr. Goulston's article describing recent advances in English medicine that "Bonney and Pickering have recently proved to most people's satisfaction that pain in peptic ulcer is due to the action of a certain degree of acidity".

Bonney and Pickering have not produced any new evidence. Their work duplicates that carried out many years ago by W. L. Palmer.

A complete analysis of the available evidence could not be compressed into a letter. But it may be stated that there is a great mass of evidence which has convinced nearly all investigators that there is no direct connexion between the pains of ulcer and the acidity of the gastric contents.

Amongst those whose evidence weighs against the acid theory are Hurst, Cook and Schlesinger (1908); Hurst (1911); C. Bolton (1913); Boring (1915); Sippy (1915); Carlson and Braafladt (1915); Ginzburg, Tumpowsky and Hamburger (1916); Carlson (1917); Hardt (1918, 1922); Reynolds and McClure (1922); Baird, Campbell and Hern (1924); Ryle (1925); Hardy (1926, 1929); Dickson and Wilson (1928); Christensen and Faber (1935); Dimitriu, Tanasoca and Popovici (1938); Alvarez (1939); Brown and Dolkart (1939); Wolf and Wolff (1943). There are many others. Amongst them are distinguished physiologists, clinicians and psychologists, all particularly interested in gastro-enterology.

In order to meet this contrary evidence, Bonney and Pickering adopted the same expedient which Palmer had adopted. They promptly dismissed the previous evidence as unreliable without showing where the errors had been made. This earned a rebuke from Alvarez, who concluded his remarks by pointing out that "Knowledge is not obtained by rejecting embarrassing data".

Evidence like that which led nearly all observers to reject the acid theory has even been collected by Bonney and Pickering. It is probably reliable. At any rate it convinced Bonney and Pickering that there must be in the gastro-duodenal wall some other factor the nature of which they cannot guess.

Yours, etc.,

235, Macquarie Street, Sydney,
July 8, 1947.

V. J. KINSELLA.

THE UNIVERSITIES COMMISSION AND THE DEFERMENT OF TRAINING.

SIR: The following statement by the Universities Commission applies in all States.

> In view of the length of time which has now elapsed since the conclusion of hostilities, the Commission has given careful consideration to the question of deferment of training and it has ruled that part-time training under Category P(b)—Improvement of Occupational Status—may be deferred on the applicant's expressed wish until the commencement of 1948 and until the commencement of 1949 if the applicant satisfies the Commission that good reasons exist therefor. With regard to full-time refresher training the Commission has ruled that deferment of the commencement date beyond the 31st December, 1947, may be granted only under special circumstances. These would include, in the case of

medical refresher training, circumstances beyond the applicant's control, such as serious illness, or an opportunity to undergo a course of training as a resident medical officer at a hospital as an introduction to a full-time medical refresher course.

We should like to draw this to the attention of ex-service medical officers.

Yours, etc.,
P. S. WOODRUFF,
Assistant Director.

Melbourne Permanent Post-Graduate Committee,
College of Surgeons,
Spring Street,
Melbourne.
July 17, 1947.

PEANUTS AND BABIES.

SIR: During the last twelve months at the Children's Hospital, Melbourne, we have had eleven children who have inhaled peanuts into the air passages, either into the trachea or a bronchus, in each case requiring endoscopic removal of the nut. Six of the patients were babies under the age of two years, the youngest being fourteen months old.

Such a number in one year is unprecedented in my twenty years' association with the hospital, and no doubt the fact that peanuts were unprocurable during the war has something to do with the large number of cases.

I am curious to know whether my colleagues in the other capital cities have had a similar experience.

Yours, etc.,
RAYMOND HENNESSY.

55, Collins Street,
Melbourne,
July 7, 1947.

Obituary.

JOHN ELLISON PORTER.

WE are indebted to Dr. P. T. S. Cherry for the following appreciation of the late Dr. John Ellison Porter.

Dr. John Ellison Porter, of Military Road, Largs Bay, South Australia, who died on April 24, 1947, was born in Adelaide fifty years ago. He attended Prince Alfred College and represented his school in football and athletics. At the age of eighteen he left school for World War I and served for four years abroad, being awarded the Military Medal. On his return to Australia he took the medical course at the University of Adelaide and graduated in 1925. He immediately entered into partnership with me at Port Adelaide, which association was maintained until his death. After his graduation Dr. Porter took an active part in the military and rose to the rank of lieutenant-colonel in charge of a field ambulance and received the Efficiency Decoration while in camp. In 1940 he enlisted for the World War II, but his health prevented his acceptance. He was the only son of the late Mr. W. H. Porter, a pharmaceutical chemist of Port Adelaide, and, like his father, took an active interest in racing. At the time of his death he was a member of the committee of the Port Adelaide Racing Club. A widow and three young children survive him.

GUY DIXON MENZIES.

WE are indebted to Sir Robert Wade for the following appreciation of the late Dr. Guy Dixon Menzies.

Guy Dixon Menzies, whose death was reported in a previous issue, was one of the early graduates from the University of Sydney Medical School, passing his final examination in 1895. After a year spent as resident medical officer at the Prince Alfred Hospital, as it was then called, he commenced practice at Drummoyne, then a small suburb on the outskirts of the city proper. There he continued his medical practice until his death, and with the suburb's growth to a thickly populated residential area his work enlarged and became very arduous. He was well liked and esteemed in the district both for his personal qualities and for the high standard of the medical attention he gave to all so generously. Essentially one of the most meticulously careful and honest types, he by wide reading kept his work up to date. He gave of his best to all his patients, to whom he was not only a trusted medical attendant but an honoured personal friend. In his young days, before surfing was known as a recreation, he was a first-class and fearless swimmer in the ocean at Coogee where he lived—a form of exercise somewhat different from bobbing up and down in the shore waves and present-day sunbaking. In those days he was a revelation to his school-boy friends and companions for his ease in the water. He was keen on rifle-shooting as a cadet at the Sydney Grammar School, where he was educated, and later was an able exponent of golf and bowls. Alert to all new interests, he was an enthusiast in the early days of wireless transmission.

He was a man devoted to his family, and his later years were saddened by tha loss of two sons serving in the air force during World War II. A lovable companion and good friend as well as an earnest and capable medical practitioner, he will be missed by his friends in the district of Drummoyne, for his long residence there of over fifty years had made him a household identity that all knew and respected.

BERNARD BALFOUR GARRETT.

WE regret to announce the death of Dr. Bernard Balfour Garrett, which occurred on July 18, 1947, at Melbourne.

LINDSAY PEREGRINE BRENT.

WE regret to announce the death of Dr. Lindsay Peregrine Brent, which occurred on July 18, 1947, at Adelaide.

JOSEPH PETER KELLY.

WE regret to announce the death of Dr. Joseph Peter Kelly, which occurred on July 20, 1947, at Melbourne.

JAMES WILLIAM KENNY.

WE regret to announce the death of Dr. James William Kenny, which occurred on July 23, 1947, at Melbourne.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Jones, Alfred Kenneth, M.B., B.S., 1939 (Univ. Sydney), 36, Manning Road, Double Bay.

Caradus, Verne, provisional registration, 1947 (Univ. Sydney), St. George District Hospital, Kogarah.

Relf, Lawrence Lardner, provisional registration, 1947 (Univ. Sydney), Ryde District Soldiers' Memorial Hospital, Eastwood.

Morton, Max Robson, provisional registration, 1947 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Harrison, Graham Grantham, provisional registration, 1947 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Creagh, Anthony, M.B., B.S., 1946 (Univ. Sydney), The Pah, River Road, Panania.

Waugh, Martin Lindsay, M.B., B.S., 1946 (Univ. Sydney), Base Hospital, Orange.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts, 1939 to 1946*, of Queensland, as duly qualified medical practitioners:

Milgate, Leslie Thomas, M.B., B.S., 1943 (Univ. Sydney), 72, New Canterbury Road, Petersham, New South Wales.

Fenton, Clyde Cornwall, M.B., B.S., 1925 (Univ. Melbourne), 26, Langside Road, Hamilton, Brisbane.
Ariotti, Louis Charles, M.B., B.S., 1941 (Univ. Sydney), Charleville.
Kearns, Daniel Philip, L.A.H., 1939 (Dublin), D.P.H., Q.U., 1942 (Belfast), c.o. the Dental Clinic, Biloela.
Hession, George Edward, M.B., B.S., 1946 (Univ. Sydney), c.o. Dr. R. P. Rundle, Rockhampton.
Green, Brian Geoffrey, M.B., 1944 (Univ. Sydney), Cairns District Hospital, Cairns.
Fraser, Allan Arthur, M.B., B.S., 1945 (Univ. Sydney), Townsville Hospital, Townsville.
Frith, Bruce Austin, M.B., B.S., 1946 (Univ. Sydney), c.o. the General Hospital, Bundaberg.

The following additional qualification has been registered:
Sands, John Robert, M.R.A.C.P., c.o. the Brisbane Clinic, Wickham Terrace, Brisbane, 1947.

THE FEDERAL MEDICAL WAR RELIEF FUND.

THE following contributions to the Federal Medical War Relief Fund have been received:

New South Wales.

A. H. Hart, £10 10s.
C. H. W. Lawes, £3 3s.
Total: £13 13s.
Grand total: £19,309 0s. 6d.

Medical Appointments.

The following honorary appointments have been made to *the Royal Adelaide Hospital, Adelaide: Physicians, Dr. F. H.* Beare and Dr. F. R. Hone. Gynæcologist, Dr. J. R. S. G. Beard. Assistant Gynæcologist, Dr. R. F. Matters. Aural *Surgeon, Dr. R. McM. Glynn. Assistant Aural Surgeon, Dr.* F. J. B. Miller. Dermatologist, Dr. W. C. T. Upton. Anæsthetist, Dr. S. R. Hecker. Assistant Anæsthetists, Dr. M. T. *Burnell, Dr. F. B. Leditschke and Dr. A. W. Wall. Surgeons,* Dr. G. H. Burnell and Dr. A. T. B. Jones. Surgeon, Sterility Clinic, Dr. W. J. W. Close. Gynæcologist, Sterility *Clinic, Dr. H. M. Fisher. Consultant Physician, Sterility* Clinic, Dr. E. McLaughlin. Medical Officer in Charge of Electrocardiograph, Dr. E. F. Gartrell. Medical Officer in *Charge of Resuscitation Unit, Dr. R. F. West. Director of* the Psychiatric Clinic, Dr. S. B. Forgan. Assistants to the Director of the Clinic, Dr. W. A. Dibden, Dr. K. F. Edwards, *Dr. J. D. Fotheringham and Dr. D. M. Salter.*

Dr. J. P. M. Droulers has been appointed government medical officer at Dunedoo, New South Wales.

Dr. A. J. Geoffroy, assistant medical officer of health, has been appointed medical officer of health, Mitchell Health District, New South Wales.

Dr. J. J. Donnellan, medical officer, has been appointed medical officer of health, Richmond-Tweed Health District, New South Wales.

Books Received.

"Human Climatology and Tropical Settlement", by Douglas H. K. Lee; The John Thomson Lecture for 1946; 1947. Brisbane: University of Queensland. 8¼" × 5½", pp. 36, with illustrations.

"A Handbook on Diseases of Children: Including Dietetics and the Common Fevers", by Bruce Williamson, M.D. (Edinburgh), F.R.C.P. (London); Fifth Edition; 1947. Edinburgh: E. and S. Livingstone, Limited. 7¼" × 4¾", pp. 420, with many illustrations. Price: 15s.

"The Practice of Mental Nursing", by May Houliston, R.G.N., R.M.N., R.F.N., with a foreword by P. K. McCowan, J.P., M.D. (Edinburgh), F.R.C.P. (London), D.P.M.; 1947. Edinburgh: E. and S. Livingstone, Limited. 7¼" × 4¾", pp. 176. Price: 7s. 6d.

"The Psychology of the Unwanted Child", by Agatha H. Bowley, Ph.D., with a foreword by S. Clement Brown, M.A.; 1947. Edinburgh: E. and S. Livingstone, Limited. 7¼" × 4¾", pp. 124. Price: 6s.

"Nutritional Disorders of the Nervous System", by John D. Spillane, B.Sc., M.D. (Wales), M.R.C.P. (London), with a foreword by George Riddoch, M.D., F.R.C.P.; 1947. Edinburgh: E. and S. Livingstone, Limited. 9¼" × 6", pp. 296, with many illustrations. Price: 20s.

"The Principles and Practice of Medicine: Originally Written by William Osler, M.D., F.R.C.P.: Designed for the Use of Practitioners and Students of Medicine", by Henry A. Christian, A.M., M.D., LL.D. (Hon.), Sc.D., Hon. F.R.C.P. (Cantab.), F.A.C.P.; Sixteenth Edition; 1947. New York and London: D. Appleton-Century Company, Incorporated. 9¼" × 6", pp. 1580. Price: $10.00.

"The Rotunda Hospital, 1745-1945", by O'Donel T. D. Browne, M.B., M.A., M.A.O. (Univ. Dublin), F.R.C.P. (I.), F.R.C.O.G.; 1947. Edinburgh: E. and S. Livingstone, Limited 9¼" × 7¼", pp 316, with many illustrations. Price: 42s.

Diary for the Month.

AUG. 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
AUG. 6.—Western Australian Branch, B.M.A.: Council Meeting.
AUG. 6.—Victorian Branch, B.M.A.: Branch Meeting.
AUG. 7.—South Australian Branch, B.M.A.: Council Meeting.
AUG. 8.—Queensland Branch, B.M.A.: Council Meeting.
AUG. 12.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUG. 12.—Tasmanian Branch, B.M.A.: Ordinary Meeting.
AUG. 18.—Victorian Branch, B.M.A.: Finance Committee.
AUG. 19.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with *the Medical Secretary of the British Medical Association,* Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie *Street, Sydney): Australian Natives' Association; Ashfield* and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company *Limited; Phœnix Mutual Provident Society.*

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; *all Institutes or Medical Dispensaries; Australian Prudential* Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South *Australia.*

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract *Practice appointments in Western Australia. All* government appointments with the exception of those of the Department of Public Health.

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